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(54) **Platenolide synthase gene**

(57) A DNA molecule isolated from *Streptomyces*

*ambofaciens* encodes the multi-functional proteins which direct the synthesis of the polyketide platenolide.

## Description

The present invention is directed to the DNA isolated from *Streptomyces ambofaciens* responsible for encoding the multi-functional proteins which direct the synthesis of the polyketide platenolide. The present invention also is directed to use of that DNA to produce compounds exhibiting antibiotic activity based on the platenolide structure, including specifically spiramycin and spiramycin analogues and derivatives.

Spiramycin is a macrolide antibiotic useful in both veterinary and human medicine produced by *Streptomyces ambofaciens* (ATCC 15154). Spiramycin is a 16-membered cyclic lactone, platenolide, with three attached sugar residues. Spiramycin's antibiotic activity is believed to be due to its inhibition of protein synthesis by a mechanism that involves binding of the antibiotic to a ribosome. Spiramycin is structurally similar to another antibiotic, tylosin, and the biosynthetic pathways of both are known to be similar.

The biosynthesis of tylosin has been thoroughly investigated (Baltz et al., *Antimicrobial Agents and Chemotherapy*, 20(2):214-225(1981); Beckmann et al., *Genetics and Molecular Biology of Industrial Microorganisms*, (1989):176-186). Polyketides are synthesized via a common mechanistic scheme thought to be related to fatty acid synthesis. The cyclic lactone framework is prepared by a series of condensations involving small carboxylic acid residues. Modifications of the structure, such as ketoreduction, dehydration and enoylreduction, also occur during the processing. The synthesis is driven by a set of large multi-functional polypeptides, referred to as polyketide synthases.

PCT Publication WO 93/13663 describes the organization of the gene encoding the polyketide synthase of *Saccharopolyspora erythraea*. The gene is organized in modules, with each module effecting one condensation step. The precise sequence of chain growth and the processing of the growing chain is determined by the genetic information in each module. This PCT application describes an approach for synthesizing novel polyketide structures by manipulating in several ways the DNA governing the biosynthesis of the cyclic lactone framework. In order to adapt this methodology to other polyketides, however, the DNA molecules directing the biosynthetic processing must first be isolated.

The present invention is directed to the DNA sequence for the gene cluster responsible for encoding platenolide synthase, the building machinery of platenolide which is the basic building block of spiramycin. As a result, the present invention provides the information needed to synthesize novel spiramycin-related polyketides based on platenolide, arising from modifications of this DNA sequence designed to change the number and type of carboxylic acids incorporated into the growing polyketide chain and to change the kind of post-condensation processing that is conducted.

The present invention provides a DNA molecule comprising an isolated DNA sequence that encodes a platenolide synthase domain. Thus, the present invention provides the DNA molecule of SEQ ID NO:1 and DNA molecules that contain submodules thereof. The present invention also provides the products encoded by said DNA molecules, recombinant DNA expression vectors, and transformed microbial host cells. The present invention is further directed to a method of screening for new antibiotics based on the platenolide structure.

Figure 1 shows the map of the *srmG* region of the *S. ambofaciens* DNA. Distances in kb are shown relative to the beginning of *srmG*. Open reading frames (ORF) are indicated by block arrows. The *srmG* DNA (0-42 kb) is the platenolide PKS region. The indicia Ap, G, E, K, P, and X denote restriction sites *Apal*, *BglII*, *EcoRI*, *KpnI*, *PstI* and *XhoI*, respectively. Predicted domains for the *srmG* DNA are labeled as shown. ACP stands for acyl carrier protein; AT stands for acyltransferase; DH stands for dehydratase; ER stands for enoylreductase; KR stands for ketoreductase; KS stands for ketosynthase; and KS' stands for a ketosynthase-like domain in which a glutamine residue is present in the position occupied by an active site cysteine in a normal ketosynthase. KR' is a domain that resembles a ketoreductase but which is predicted to be inactive.

Figure 2 demonstrates the biosynthetic pathway for platenolide synthesis. A denotes malonyl-CoA; B denotes ethylmalonyl-CoA; P denotes methylmalonyl-CoA; C2 denotes a CoA derivative related to malonyl-CoA but of unknown structure.

Figure 3 shows the map of two clones that span the whole region of the *srmG* DNA.

The term polyketide defines a class of molecules produced through the successive condensation of small carboxylic acids. This diverse group includes plant flavonoids, fungal aflatoxins, and hundreds of compounds of different structures that exhibit antibacterial, antifungal, antitumor, and anthelmintic properties. Some polyketides produced by fungi and bacteria are associated with sporulation or other developmental pathways; others do not yet have an ascribed function. Some polyketides have more than one pharmacological effect. The diversity of polyketide structures reflects the wide variety of their biological properties. Many cyclized polyketides undergo glycosidation at one or more sites, and virtually all are modified during their synthesis through hydroxylation, reduction, epoxidation, etc.

A common feature of compounds in this class is that their synthesis is directed by a complex of multi-functional peptides, termed a "polyketide synthase". Molecular genetic analysis of polyketide synthase genes has revealed two distinct classes of enzymes operating for different polyketides: (a) the aromatics, which are made through an essentially iterative process; (b) the complex polyketides, which comprise several repeats of the same activities arranged in few, very large polypeptides. A common feature among complex polyketide synthase genes is that they are generally arranged in several open reading frames (ORFs), each of which contains one or more repeated units, designated mod-

ules. Each module processes one condensation step and typically requires several activities accomplished by several enzymes including acyl carrier protein (ACP),  $\beta$ -ketosynthase (KS), and acyltransferase (AT).

Therefore a "module" is defined as the genetic element encoding a multi-functional protein segment that is responsible for all of the distinct activities required in a single round of synthesis, i.e., one condensation step and all the  $\beta$ -carbonyl processing steps associated therewith. Each module encodes an ACP, a KS, and an AT activity to accomplish the condensation portion of the synthesis, and selected post-condensation activities to effect  $\beta$ -carbonyl processing. Each module is therefore, further characterized by the inclusion of submodules that are responsible for encoding the distinct activities of a complex polyketide synthase. A "submodule" thus is defined as the portion of the polyketide synthase DNA sequence that encodes a distinct activity, or "domain". A distinct activity or domain is commonly understood to mean that part of the polyketide synthase polypeptide necessary for a given distinct activity.

The protein segments corresponding to each module are called synthase units (SUs). Each SU is responsible for one of the fatty acid-like cycles required for completing the polyketide; it carries the elements required for the condensation process, for selecting the particular extender unit (a coenzyme A thioester of a dicarboxylate) to be incorporated, and for the extent of processing that the  $\beta$ -carbon will undergo. After completion of the cycle, the nascent polyketide is transferred from the ACP it occupies to the KS of the next SU utilized, where the appropriate extender unit and processing level are introduced. This process is repeated, employing a new SU for each elongation cycle, until the programmed length has been reached. As in synthesis of long chain fatty acids, the number of elongation cycles determines the length of the molecule. However, whereas fatty acid synthesis involves a single SU used iteratively, formation of complex polyketides requires participation of a different SU for each cycle, thereby ensuring that the correct molecular structure is produced. The composition of the polyketide synthase gene modules are variable. Some carry the full complement of  $\beta$ -ketoreductase(KR), dehydratase(DH), and enoylreductase(ER) domains, and some encode a particular domain only or lack a functional domain, although much of the sequence is preserved.

This variable composition of the modules, which correlate with the asymmetry in the synthesis of the polyketide precursor, enable a specific step to be assigned to each module. Since each enzymatic activity is involved in a single biochemical step in the pathway, loss of any one activity should affect only a single step in the synthesis. Knowledge of the correlation between the structure of the polyketide and the organization of the polyketide synthase genes enables one to produce altered genes selectively which produce a polyketide derivative with predicted structure.

Because the degree of processing appears to depend on the presence of functional domains in a particular SU, inactivation of a KR, DH, or ER will result in a polyketide less processed at a single site, but only if the altered chain thus produced can be utilized as a substrate for the subsequent synthesis steps. Thus, the inactivation of one of these domains should result in the formation of a polyketide retaining a ketone, hydroxyl, or site of unsaturation at the corresponding position. This rationale has led to the successful production of altered erythromycin derivatives from strains in which a KR or an ER domain had been inactivated.

Thus, one can engineer polyketide pathways by genetic intervention of the polyketide synthase and by adding or eliminating modification steps. Many of the enzymes involved in postpolyketide modifications do not seem to have absolute specificity for a particular structure. In addition one can also select the desired components from a library of polyketide and postpolyketide biosynthesis genes and combine them to produce novel structures.

The present invention provides, in particular, the DNA sequence encoding the polyketide synthase responsible for biosynthesis of platenolide, i.e., platenolide synthase. Platenolide itself is the foundation for spiramycin-related polyketides. The platenolide synthase DNA sequence, which defines the platenolide synthase gene cluster, directs biosynthesis of the platenolide polyketide by encoding the various distinct activities of platenolide synthase.

The gene cluster for platenolide synthase, like other polyketide biosynthetic genes whose organization has been elucidated, is characterized by the presence of several ORFs, each of which contains one or more repeated units termed modules as defined above. Each module also further includes submodules as defined above. Organization of the platenolide synthase gene cluster derived from *Streptomyces ambofaciens* is shown in Figure 1. The accompanying synthetic pathway and the specific carboxylic acid substrates that are used for each condensation reaction and the post-condensation activities of platenolide synthase are indicated in Figure 2.

A preferred DNA molecule comprising the platenolide synthase gene cluster isolated from *Streptomyces ambofaciens* is represented by SEQ ID NO: 1. Other preferred DNA molecules of the present invention include the various ORFs of SEQ ID NO: 1 that encode individual multi-functional polypeptides. These are represented by ORF1, 350 to 14002, ORF2, 14046 to 20036, ORF3, 20110 to 31284, ORF4, 31329 to 36071, and ORF5, 36155 to 41830 all in SEQ ID NO: 1. The predicted amino acid sequences of the various peptides encoded by these sequences are shown in SEQ ID NO: 2, 3, 4, 5, and 6.

Yet other preferred DNA molecules of the present invention include the modules that encode all the activities necessary for a single round of synthesis. These are represented by starter module 392 to 3424, module 1, 3527 to 8197, module 2, 8270 to 13720, module 3, 14148 to 19730, module 4, 20215 to 24678, module 5, 24742 to 31002, module 6, 31428 to 35837, and module 7, 36257 to 41395 all in SEQ ID NO: 1. The predicted amino acid sequences of the various synthase units encoded by these modules are represented by starter SU 15 to 1025, SU1, 1060 to 2616,

and SU2, 2641 to 4457 in SEQ ID NO: 2; SU3, 35 to 1895 in SEQ ID NO: 3; SU4, 36 to 1523, and SU5, 1545 to 3631 in SEQ ID NO: 4; SU6, 34 to 1503 in SEQ ID NO: 5; SU7, 35 to 1747 all in SEQ ID NO: 6.

Still other preferred DNA molecules include the various submodules that encode the various domains of platenolide synthase. These submodules are represented by KS'(s), 392 to 1603, AT(s), 1922 to 2995, and ACP(s), 3173 to 3424 of starter module in SEQ ID NO:1; KS1, 3527 to 4798, AT1, 5135 to 6208, KR1, 7043 to 7597, and ACP1, 7946 to 8197 of module 1 in SEQ ID NO: 1; KS2, 8270 to 9541, AT2, 9899 to 10909, DH2, 10985 to 11530, KR2, 12596 to 13153, and ACP2, 13469 to 13720 of module 2 in SEQ ID NO: 1; KS3, 14148 to 15422, AT3, 15789 to 16844, DH3, 16914 to 17510, KR3, 18612 to 19166, and ACP3, 19479 to 19730 of module 3 in SEQ ID NO: 1; KS4, 20215 to 21486, AT4, 21889 to 22872, KR4, 23638 to 24159, and ACP4, 24484 to 24678 of module 4 in SEQ ID NO: 1; KS5, 24742 to 26016, AT5, 26371 to 27381, DH5, 27442 to 27966, ER5, 28843 to 29892, KR5, 29905 to 30462, and ACP5, 30760 to 31002 of module 5 in SEQ ID NO: 1; KS6, 31428 to 32696, AT6, 33024 to 34022, KR6, 34770 to 35327, and ACP6, 35586 to 35837 of module 6 in SEQ ID NO: 1; KS7, 36257 to 37528, AT7, 37898 to 38905, KR7, 39851 to 40408, ACP7, 40658 to 40909, and TE, 41297 to 41395 of module 7 in SEQ ID NO: 1. The predicted amino acid sequences of the various domains encoded by these submodules are represented by KS'(s), 15 to 418, AT(s), 525 to 882, and ACP(s), 942 to 1025 of starter SU in SEQ ID NO:2; KS1, 1060 to 1483, AT1, 1596 to 1953, KR1, 2232 to 2416, and ACP1, 2533 to 2616 of SU1 in SEQ ID NO: 2; KS2, 2641 to 3064, AT2, 3184 to 3520, DH2, 3546 to 3727, KR2, 4083 to 4268, and ACP2, 4374 to 4457 of SU2 in SEQ ID NO: 2; KS3, 35 to 459, AT3, 582 to 933, DH3, 957 to 1155, KR3, 1523 to 1707, and ACP3, 1812 to 1895 of SU3 in SEQ ID NO: 3; KS4, 36 to 459, AT4, 594 to 921, KS4, 1177 to 1350, and ACP4, 1459 to 1523 of SU4 in SEQ ID NO: 4; KS5, 1545 to 1969, AT5, 2088 to 2424, DH5, 2445 to 2619, ER5, 2912 to 3261, KR5, 3266 to 3451, and ACP5, 3551 to 3631 of SU5 in SEQ ID NO: 4; KS6, 34 to 456, AT6, 566 to 898, KR6, 1148 to 1333, and ACP6, 1420 to 1503 of SU6 in SEQ ID NO: 5; KS7, 35 to 458, AT7, 582 to 917, KR7, 1233 to 1418, ACP7, 1502 to 1585, and TE, 1715 to 1747 of SU7 in SEQ ID NO: 6.

Although not wishing to be bound to any particular technical explanation, a sequence similarity exists among domain boundaries in various polyketide synthase genes. Thus, one skilled in the art is able to predict the domain boundaries of newly discovered polyketide synthase genes based on the sequence information of known polyketide synthase genes. In particular, the boundaries of submodules, domains, and open reading frames in the instant application are predicted based on sequence information disclosed in this application and the locations of the domain boundaries of the erythromycin polyketide synthase (Donadio et al., *GENE*, 111 51-60 (1992)). Furthermore, the genetic organization of the platenolide synthase gene cluster appears to correspond to the order of the reactions required to complete synthesis of platenolide. This means that the polyketide synthase DNA sequence can be manipulated to generate predictable alterations in the final platenolide product.

The DNA sequence of the platenolide synthase gene can be determined from recombinant DNA clones prepared from the DNA of *Streptomyces ambofaciens*, in particular strain ATCC 15154. The platenolide synthase gene is contained in recombinant DNA vectors pKC1080 and pKC1306 (Figure 1), which are available from the National Center for Agricultural Utilization Research, 1815 North University Street, Peoria, Illinois 61604-3999, in *E. coli* DH10B under accession numbers B-21500 for pKC1080 (deposited Sep 21, 1995) and B-21499 for pKC1306 (deposited Sep 21, 1995) respectively.

Techniques of isolating bacterial DNA are readily available and well known in the art. Any such techniques can be employed in this invention. In particular DNA from these deposited cultures can be isolated as follows. Lyophils of *E. coli* DH10B/pKC1080 or *E. coli* DH10B/pKC1306 are plated onto L-agar (10 g tryptone, 10 g NaCl, 5 g yeast extract, and 15 g agar per liter) plates containing 100 µg/ml apramycin to obtain a single colony isolate of the strain. This colony is used to inoculate about 500 ml of L-broth (10 g tryptone, 10 g NaCl, 5 g yeast extract per liter) containing 100 µg/ml apramycin, and the resulting culture is incubated at 37°C with aeration until the cells reach stationary phase. Cosmid DNA can be obtained from the cells in accordance with procedures known in the art (see e.g., Rao et al., 1987 in *Methods in Enzymology*, 153:166).

DNA of the current invention can be sequenced using any known techniques in the art such as the dideoxynucleotide chain-termination method (Sanger, et al., *Proc. Natl. Acad. Sci.* 74:5463 (1977)) with either radioisotopic or fluorescent labels. Double-stranded, supercoiled DNA can be used directly for templates in sequence reactions with sequence-specific oligonucleotide primers. Alternatively, fragments can be used to prepare libraries of either random, overlapping sequences in the bacteriophage M13 or nested, overlapping deletions in a plasmid vector. Individual recombinant DNA subclones are then sequenced with vector-specific oligonucleotide primers. Radioactive reaction products are electrophoresed on denaturing polyacrylamide gels and analyzed by autoradiography. Fluorescently labeled reaction products are electrophoresed and analyzed on Applied Biosystems (ABI Division, Perkin Elmer, Foster City, CA 94404) model 370A and 373A or Dupont (Wilmington, DE) Genesis DNA sequencers. Sequence data are assembled and edited using Genetic Center Group (GCG, Madison, WI) programs GelAssemble and SeqEd or the ABI model 670 Inherit Sequence Analysis system and the AutoAssembler and SeqEd programs.

Polypeptides corresponding to a domain, a submodule, a module, a synthesis unit (SU), or an open reading frame can be produced by transforming a host cell such as bacteria, yeast, or eukaryotic cell-expression system with the

cDNA sequence in a recombinant DNA vector. It is well within one skilled in the art to choose among host cells and numerous recombinant DNA expression vectors to practice the instant invention. Multifunctional polypeptides of polyketide platenolide synthase can be extracted from platenolide-producing bacteria such as *Streptomyces ambofaciens* or translated in a cell-free in vitro translation system. In addition, the techniques of synthetic chemistry can be employed to synthesize some of the polypeptides mentioned above.

Procedures and techniques for isolation and purification of proteins produced in recombinant host cells are known in the art. See, for example, Roberts et al., Eur. J. Biochem. 214, 305-311, (1993) and Caffrey et al., FEBS 304, 225-228 (1992) for detailed description of polyketide synthase purification in bacteria. To achieve a homogeneous preparation of a polypeptide, proteins in the crude cell extract can be separated by size and/or charge through different columns well known in the art once or several times. In particular the crude cell extract can be applied to various cellulose columns commercially available such as DEAE-cellulose columns. Subsequently the bound proteins can be eluted and the fractions can be tested for the presence of the polyketide platenolide synthase or engineered derivative protein. Techniques for detecting the target protein are readily available in the art. Any such techniques can be employed for this invention. In particular the fractions can be analysed on Western blot using antibodies raised against a portion or portions of such polyketide platenolide synthase proteins. The fractions containing the polyketide platenolide synthase protein can be pooled and further purified by passing through more columns well known in the art such as applying the pooled fractions to a gel filtration column. When visualized on SDS-PAGE gels homogeneous preparations contain a single band and are substantially free of other proteins.

Knowledge of the platenolide synthase DNA sequence, its genetic organization, and the activities associated with particular open reading frames, modules, and submodules of the gene enables production of novel polyketides having a predicted structure that are not otherwise available. Modifications may be made to the DNA sequence that either alter the initial carboxylic acid building block used or alter the building block added at any of the condensation steps. The platenolide synthase gene may also be modified to alter the actual number of condensation steps done, thereby changing the size of the carbon backbone. Submodules that are part of the present invention may be selectively inactivated thereby giving rise to predictable, novel polyketide structures. Modifications to portions of the DNA sequence that encode the post-condensation processing activities will alter the functional groups appearing at the various condensation sites on the carbon chain backbone.

One skilled in the art is fully familiar with the degeneracy of the genetic code. Consequently, the skilled artisan can modify the specific DNA sequences provided by this disclosure to provide proteins having the same or improved characteristics compared to those polypeptides specifically provided herein. Also, one skilled in the art can modify the DNA sequences to express an identical protein to those provided, albeit expressed at higher levels. Furthermore, one skilled in the art is familiar with means to prepare synthetically, either partially, or in whole, DNA sequences which would be useful in preparing recombinant DNA vectors or coding sequences which are encompassed by the current invention. Additionally, recombinant means for modifying the DNA sequences provided may include for example site-directed deletion or site-directed mutagenesis. These techniques are well known to those skilled in the art and require no further elaboration here. Consequently, as used herein, DNA which is isolated from natural sources, prepared synthetically or semi-synthetically, or which are modified by recombinant DNA methods, are within the scope of the present invention.

Likewise, those skilled in the art will recognize that the polypeptides of the invention may be expressed recombinantly. Alternatively, these polypeptides may be synthesized as well, either in whole or in part, by conventional known non-recombinant techniques; for example, solid-phase synthesis. Thus, the present invention should not be construed as necessarily limited to any specific vector constructions or means for production of the specific polyketide synthase molecules exemplified. These alternate means for preparing the present polypeptides are meant to be encompassed by the present invention.

Many cyclized polyketides undergo glycosidation at one or more sites. Spiramycin is a 16-membered cyclic lactone, platenolide, with three attached sugar residues. The process of converting platenolide to spiramycin is well known in the art. The present invention also provides the information needed to synthesize novel spiramycin-related polyketides based on platenolide. The principles have already been described above. In addition, any product resulting from post-transcriptional or post-translational modification in vivo or in vitro based on the DNA sequence information disclosed here are meant to be encompassed by the present invention.

The following example is provided for exemplification purposes only and is not intended to limit the scope of the invention which has been described in broad terms above.

#### Example 1:

##### Specific experimental details and results from the sequencing of platenolide synthase.

The DNA sequence of the *S. ambofaciens* platenolide synthase (srmG) gene can be obtained by sequencing inserts of recombinant DNA subclones containing contiguous or overlapping DNA segments of the region indicated in

Figure 3. All sequences representing srmG are fully contained in the overlapping cosmid clones pKC1080 and pKC1306 (Figure 3). The sequence can be obtained by subcloning and sequencing the fragments bounded by NruI sites at position 1, 0.3 kb, 8.2 kb, 14.1 kb, 20.2 kb, 29.5 kb, 31.4 kb, 41.1 kb and 42.0 kb. In order to obtain the srmG region on a single fragment, the 25.0 kb fragment bounded by the NruI site at position 1 and the SfuI site at 25.0 kb should be isolated from a partial digestion of pKC1080 with restriction enzymes NruI and SfuI. The 17.8 kb DNA fragment bounded by the SfuI sites at 25.0 kb and 42.8 kb should be isolated from a digestion of pKC1306 with the restriction enzyme SfuI. The resulting fragments should be ligated and cloned in an appropriate recombinant DNA vector. Clones containing the correct orientation of the two ligated fragments can be identified by restriction enzyme site mapping.

The principles, preferred embodiments and modes of operation of the present invention have been described in the foregoing specification. The invention which is intended to be protected herein, however, is not to be construed as limited to the particular forms disclosed, since they are to be regarded as illustrative rather than restrictive. Variations and changes may be made by those skilled in the art without departing from the spirit of the invention.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: ELI LILLY AND COMPANY  
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 (F) ZIP: 46285

(ii) TITLE OF INVENTION: PLATENOLIDE SYNTHASE GENE

(iii) NUMBER OF SEQUENCES: 6

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 (C) CITY: Windlesham  
 (D) STATE: Surrey  
 (E) COUNTRY: United Kingdom  
 (F) ZIP: GU20 6PH

(v) COMPUTER READABLE FORM:  
 (A) MEDIUM TYPE: Floppy disk  
 (B) COMPUTER: Macintosh  
 (C) OPERATING SYSTEM: Macintosh 7.0  
 (D) SOFTWARE: Microsoft Word 5.1

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 44377 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:  
 (A) NAME/KEY: CDS  
 (B) LOCATION: 350..14002

(ix) FEATURE:  
 (A) NAME/KEY: CDS

(B) LOCATION: 14046..20036

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 20110..31284

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 31329..36071

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 36155..41830

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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	GAAATCTTCT CCGCTCGCCC AGGACTCCGC GTGCAGGTCA CCGAGTGCG CGACCGGCCG	120
	GGACGTCGGA GCGCCGACCC TCGGACCTG GTGCGATGCC GTGTGGTCCC GCATGATCCC	180
	GCGCCGTCTC CGGTGACGAG AATCGGTGGA CAATCTCCGA ACTTGACACA ATTGATTGTC	240
	GTTCACCGGC CGTTCCTGTC GCGCGCAGT TCGCCCGCTG TACGCTCGGG AAGATCAAGA	300
	AAAGGCAGAA AAGCCACGGC GTGGTACGGC GAACATATGA GGGATGCAGG TGTCTGGAGA	360
	ACTCGCGATT TCCCGCAGTG ACGACCGGTC CGACGCCGTT GCCGTGGTCG GAATGGCGTG	420
	CCGGTTTCCC GCGCCCCCGG GAATTGCCGA ATTCTGAAA CTGCTGACCG ACGGAAGGGA	480
	CGCGATCGGC CGGACGCGG ACGGCCGCG GCGCGGCATG ATCGAGGCGC CCGGCGACTT	540
	CGACGCCGCC TTCTTCGGCA TGTCACCCCG CGAGGCCGCC GAGACCGACC CCCAGCAGCG	600
	CCTGATGCTC GAACTCGGCT GGGAGGCTCT GGAGGACGCC GGCATCGTCC CCGGCTCCCT	660
	GCGCGGCGAG GCGGTGGCG TCTTCGTGCG GGCCATGCAC GACGACTACG CCACCCTGCT	720
	CCACCGCGCC GCGCGCGCG TCGGCCCCCA CACCGCCACC GGCCTCCAGC GCGCCATGCT	780
	CGCCAACCGG CTCTCCTACG TCCTGGGGAC GCGCGGCCCC AGCCTCGCGG TCGACACCGC	840
	CCAGTCGTCC TCCCTGGTCG CCGTGGCCCT CGCCGTCGAG AGCCTGCGGG CCGGCACCTC	900
	CCGCGTCGCC GTCGCGGGG GCGTCAACCT GGTCTCGCC GACGAGGAA CGGCCGCCAT	960
	GGAACGCCTC GCGCGCTGT CACCCGACGG CCGCTGCCAC ACCTTCGACG CCCGTGCCAA	1020
	CGGCTATGTC CGCGGTGAGG GCGGCGCCGC CGTCGTCCTG AAGCCCCTCG CCGACGCCCT	1080
	GGCCGACGGG GACCCCGTGT ACTGCGTGGT GCGTGGCGTC GCCGTCGGCA ACGACGGCGG	1140
	CGGCCCCGGG CTGACCGCTC CCGACCGCGA GGGACAGGAG GCGGTGCTCC GGGCCGCCTG	1200
	CGCCCAGGCC CCGGTCGACC CCGCCGAGGT GCGTTTCGTC GAACTGCACG GCACGGGAAC	1260



## EP 0 791 656 A2

	CCCCGTGGGC	GACCCGGTCG	AGGCACACGC	CCTCGGCGCG	GTGCACGGCT	CCGGTCGGCC	1320
	GGCCGACGAC	CCCCTGCTGG	TGGGGTCGGT	GAAGACCAAC	ATCGGCCACC	TGGAGGGCGC	1380
5	CGCCGGCATC	GCGGGCCTGG	TCAAGGCCGC	ACTGTGCCTG	CGGGAACGCA	CCCTTCCCGG	1440
	CTCGCTGAAC	TTCGCCACCC	CCTCTCCGGC	CATCCCGCTG	GACCAGCTCC	GGCTGAAGGT	1500
10	GCAGACCGCT	GCCGCCGAGC	TGCCGCTCGC	CCCGGGCGGC	GCACCCCTGC	TGGCGGGTGT	1560
	CAGTTCGTTC	GGCATCGGTG	GCACCAACTG	CCATGTGGTC	CTGGAACACC	TGCCCTCCCG	1620
	GGCCACCCCG	GCCGTCTCCG	TCGCCGCCTC	GCTTCCGGAC	GTCCCGCCGC	TGTTGTTGTC	1680
15	CGCGCGGTGC	GAGGGGGCGT	TGCGGGCGCA	GGCGGTGCGG	TTGGGTGAGT	ACGTGGAGCG	1740
	GGTGGGCGCG	GATCCGCGGG	ATGTGGCTTA	TTCGCTGGCT	TCGACGCGGA	CTCTTTTCGA	1800
	GCACCGTGCG	GTGGTGCCGT	GTGGTGGGCG	TGGGGAGCTC	GTGCTGCTC	TTGGTGGGTT	1860
20	TGCTGCCGGG	AGGGTGTCG	GGGGTGTCG	GTCCGGGCGG	GCTGTGCCGG	GTGGGGTGGG	1920
	GGTGTGTGTC	ACGGGTCAGG	GTGCGCAGTG	GGTTGGTATG	GGGCGTGGGT	TGTATGCGGG	1980
25	GGGTGGGGTG	TTTGCGGAGG	TGCTGGATGA	GGTGTGTGCG	ATGGTGGGGG	AGGTGGATGG	2040
	TCGGTCGTTG	CGGGATGTGA	TGTTCCGGCA	CGTCGACGTG	GACGCGGGTG	CCGGGGCTGA	2100
	TGCGGGTGCC	GGTGCGGGTG	CTGGGGTCCG	TTCTGGTTCC	GGTTCTGTGG	GTGGGTTGTT	2160
30	GGGTCCGACG	GAGTTTGCTC	AGCCTGCGTT	GTTTGCGTTG	GAGGTGGCGT	TGTTCCGGGC	2220
	GTTGGAGGCT	CGGGGTGTGG	AGGTGTCGGT	GGTGTGCGGT	CATTCGGTGG	GGGAGGTGGC	2280
	TGCTGCGTAT	GTGGCGGGGG	TGTTGTCGTT	GGGTGATGCG	GTGCGGTTGG	TGGTGGCGCG	2340
35	GGGTGGGTTG	ATGGGTGGGT	TGCCCGTGGG	TGGGGGGATG	TGGTCCGTGG	GGGCGTCCGA	2400
	GTGCGTGGTG	CGGGGGGTTG	TTGAGGGGTT	GGGGGAGTGG	GTGTCCGTTG	CGGCGGTGAA	2460
40	TGGCCCGCGG	TCGGTGGTGT	TGTCGGGTGA	TGTGGGTGTG	CTGGAGTCCG	TGGTTGCCCTC	2520
	GCTGATGGGG	GATGGGGTGG	AGTGCCGGCG	GTTGGATGTG	TCGCATGGGT	TTCAATTCGGT	2580
	GTTGATGGAG	CCGGTGTGTT	GGGAGTTCCG	GGGGGTTGTG	GAGTCGTTGG	AGTTCGGTTCG	2640
45	GGTGCGGCCG	GGTGTGGTGG	TGGTGTCCGG	TGTGTCCGGT	GGGGTGGTGG	GTTCCGGGGA	2700
	GTTGGGGGAT	CCGGGTATT	GGGTGCGTCA	TGCGCGGGAG	GCGGTGCGTT	TCGCGGATGG	2760
	GGTGGGGGTG	GTGCGTGGTC	TGGGTGTGGG	GACGTTGGTG	GAGGTGGGTC	CGCATGGGGT	2820
50	GCTGACGGGG	ATGGCGGGTG	ACTGCCTGGG	GGCCGGTGAT	GATGTGGTGG	TGGTGCCGGC	2880
	GATGCGGCGG	GGCCGTGCGG	AGCGGGAGGT	GTTTCGAGGCG	GCGCTGGCGA	CGGTGTTTAC	2940
55	CCGGGACGCC	GGCCTGGACG	CCACGGCACT	CCACACCGGG	AGCACCGGCC	GGCGCATCGA	3000
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	CACGGCCGAC	GCCGGGGCGG	GTGTGACCGC	CACCGATGCC	GTGGGGCACA	GCGTCTCCCC	3120
5	GGACCCGGAG	AGCACCGAGG	GGACGTCCCA	CAGGGACACG	GACGACGAGG	CGGACTCGGC	3180
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	CGTCCTGGGC	CACGACGATC	CCGGCGAGGT	CGCGCTCGAC	CGCACCTTCA	CCTCCCAGGG	3300
10	CATGGACTCG	GTGACCGCGG	TCGAGCTGTG	CGACCTGCTG	AAGGGCGCCT	CGGGGCTCCC	3360
	CCTCGCCGCC	ACGCTGGTCT	ACGACCTGCC	CACCCCGCGT	GCCGTGCGCG	AGCACATCGT	3420
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15	CGCGGTAGGG	GTGTCGGACG	CCCGGGGCGG	CAGCCGGGAC	GACGACGACC	CGATCGCCAT	3540
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25	GGCCATGGAC	CCGCAGCAGC	GCTTGCTGCT	GGAAGCGTCG	TGGGAGGCC	TCGAGGACGC	3840
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30	CGGCACCACC	GCGAGCGTGG	CCTCCGGCCG	GATCGCCTAC	ACCCCTCGGCA	CCGGCGGACC	4020
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35	GGCGCTGCGC	CGGGGCGAGT	GCGGGCTGGC	TCTGGCGGGC	GGCGCCACGG	TGATGTGCGG	4140
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EP 0 791 656 A2

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	CCACCTATGG CAGTGAGCGC CAGGGCCAAG GTCCGTTGTG GTTGGGGTCG TTGAAGTCGA	15180
50	ACATCGGGCA TGCGCAGGCG GCTCGGGGTG TGGGTGGCGT GATCAAGGTG GTGCAGGCGA	15240
	TGCGGCATGG GTCGTTGCCG CGGACGCTGC ATGTGGATGC GCCGTCGTCG AAGGTGGAGT	15300
	GGGCTTCGGG TGCGGTGGAG CTGCTGACCG AGACCCGGTC GTGGCCCGCG CGGGTGGAGC	15360
55	GGGTGCGGCG GGCCGCGGTG TCGCGGTTGC GGGTGAGCGG GACCAACGCC CATGTGCTCC	15420



	TGGAGGAAGC GCCGGCGGAG GCCGGGAGCG AGCACGGGA CGGCCCTGAA CCCGAGCGGC	15480
5	CCGACCGCGT GACGGGTCCG TTGTCTGTGG TGCTTTCTGC GCGGTCCGAG GGGGCGTTGC	15540
	GGGCGCAGGC GGTGCGGTTG CGTGAGTGTG TGGAGCGGGT GGTGCGGAT CCGCGGGATG	15600
	TGGCGGGGTC GTTGGTGGTG TCGCGTCCGT CGTTCCGTGA GCGTGCGGTG GTGGTGGGCC	15660
10	GGGGGCGTGA GGAGTTGCTG GCGGGTCTGG ATGTGGTGGC TGCCGGGGCT CCTGTGGGTG	15720
	TGTCCGGGGG CGTGTCTTCG GGGGCCGGTG CTCTGTGTCG GGGGAGTGC GTCCGGGGTC	15780
	GTCCGGTGGG GGTGTTGTTC ACGGGTCAGG GTGCGCAGTG GGTGGTATG GGGCGTGGGT	15840
15	TGTATGCGGG GGTGGGGTG TTTGCGGAGG TGCTGGATGA GGTGTTGTCT GTGGTGGGGG	15900
	AGGTGGGGGG TTGGTCTGTT CCGGATGTGA TGTTCCGCGA CGTCGACGTG GACGCGGGTG	15960
	CCGGGGCTGA TGCGGGTGTC GGTTCGGGTG TTGGTGTGGG TGGGTTGTTG GGTCCGACCG	16020
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	GGGGTGTGGA GGTGTCCGTG GTGTTGGGTC ATTCGGTGGG GGAGGTGGCT GCTGCGTATG	16140
25	TGGCGGGGGT GTTGTCTGTT GGTGATGCGG TGCGGTGCGT GGTGCGCGCG GGTGGGTTGA	16200
	TGGGTGGGTT GCCCGTGGGT GGGGGGATGT GGTCCGTGGC GCGCTCGGAG TCGGTGGTGC	16260
	GGGGGGTTGT TGAGGGGTTG GGGGAGTGGG TGTCGGTTGC GCGCGTGAAT GGGCCGCGGT	16320
30	CGGTGGTGTT GTCGGGTGAT GTCCGTGTGC TGGAGTCCGT GGTTCCTCG CTGATGGGGG	16380
	ATGGGGTGA GTGCCCGCGG TTGGATGTGT CGCATGGGTT TCATTCCGTG TTGATGGAGC	16440
	CGGTGTTGGG GGAGTTCCGG GGGGTTGTGG AGTCGTTGGA GTTCCGTCCG GTGCGGCCCG	16500
35	GTGTGGTGGT GGTGTCCAGT GTGTCCGGTG GGTGCTGGG TTCGGGGAG TTGGGGGATC	16560
	CGGGGTATTG GGTGCGTCAT GCGCGGGAGG CCGTCCGTTT CCGCGATGGG GTGGGGGTGG	16620
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40	TGGCGGGTGA GTGCCTGGGG GCCCGTGATG ATGTGGTGGT GGTGCCGGCG ATGCGGCGGG	16740
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50	CCGGCACCGA CACCGAGGTG TGGACCGGCC GCATATCCGC TGCCGACCTG CCCTGGCTCG	17040
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	TCCAGGTGGG AAGCCGGATC GGTCTGCCGC GCGTCCCGA ACTGGTCTG GAGACGCCGC	17160
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	CCCCCGGGG	CGCGCGTGAG	CTGACCCCTCC	ACTCGCGGCC	CGAGCCCGTG	GCCGCCTCCT	17280
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	GGACCCGGCA	TGCCTCAGGG	CTGCTCGCCC	CGGCTGCCGG	CCTCGCCGAC	GACTTCGCCG	17400
	AGCTCACCGG	CGCCTGGCCC	CCCGTCGGCG	CCGAGCCCTT	CGACCTCGCC	GGTCAGTACC	17460
10	CGCTCTTCGC	AGCCGCCGGA	GTGCGCTACG	AAGGCGCCTT	CCGAGGGCTG	CGCGCGGCAT	17520
	GGCGTCGAGG	CGACGAGGTC	TTCGCCGACG	TACGGCTGCC	CGACGCGCAC	GCGGTCGACG	17580
15	CTGATCGTTA	CGGGGTGCAC	CCCGCCCTGC	TCGACGCGGT	GCTCCACCCG	ATCGCGTCGC	17640
	TGGACCCGCT	GGGCGACGGC	GGGCACGGTC	TGCTGCCGTT	CTCCTGGACC	GACGTACAGG	17700
	GACACGGCGC	CGGCGGACAC	GCCCTCCGGG	TACGGGTGGC	GGCCGTCGAC	GGCGGCGCGG	17760
20	TGTCGGTCAC	CGCGGCCGAC	CACGCGGGCA	ACCCGGTGTT	ATCCGCCCCG	TCCCTGGCAC	17820
	TGCGTCGTAT	CACCGCGGAC	CGGCTTCCCG	CCGCGCCCGT	CGCCCTCTC	TACCGCGTGG	17880
	ACTGGCTGCC	GTTCCCGGGT	CCGGTGCCCG	TATCCGCGGG	CGGCCGCTGG	GCGGTCGTCG	17940
25	GACCCGAGGC	CGAAGCCACG	GCTGCCGGAC	TGCGTGCGGT	GGGCCTCGAC	GTGCGTACCC	18000
	ATGCGCTCCC	CCTCGGAGAG	CCCCTGCCTC	CGCAGGCCCG	TACCGACGCG	GAGGTGATCA	18060
	TCCTCGACCT	GACCACCACC	GCAGCCGGCC	GTACGGCGTC	GGACGGGGGG	CGGCTCAGTC	18120
30	TCCTCGACGA	GGTGCGTGCG	ACGGTGCGCC	GGACCCTCGA	AGCCGTACAG	GCCCGCCTCG	18180
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35	CCCGTACAAG	CCCCCGCGTG	GACACCCGCA	CGGGAGCCCG	CACCGCTGAC	GGCCCCCGGC	18300
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40	TGGACGTGGA	CGGCACCCAG	GCGTCGCTGC	GGGCCCTGCC	CGGTCTGCTG	GCCACGGATG	18480
	CCGGCCAGTC	GGCCGTGCGC	GACGGACGTG	TCACCGTCCC	GCGCCTCGTC	CCGGTGGCCG	18540
	ACCCCGTCCC	CCACGGCGGC	GGCACGGGGC	CCGACGGGAC	GGGTGCCGGC	GAGCCGTCCG	18600
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	3AAACCGCCCG	GCACCTGGTC	GACCGGCACA	AGGTGCGCCA	TCTCCTGCTG	GTGGGCAGGC	18720
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50	AGGTGCGCCGT	ACGGGCCTGT	GACGTCAAGG	ACCGCGACGC	CCTGCGCCGC	CTGCTCGACG	18840
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	CCGCCGTCCA CCTGGACGAG CTGACCCGGG AGATCGGACG GGTGCCCCCTG GTGCTGTACT	19020
	CCTCGGTCTC GGCCACCCTG GGCAGCGCGG GGCAGGCCCG GTACGCGGCG GCCAACGCCT	19080
5	TCATGGACGC GCTGGCCGCC CGGCGGTGCG CCGCCGGGCA CCCCAGCTG TCGCTCGGCT	19140
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	CGCTGACCCG GCCCGAGCCG GCCCTGCTGC CCGTCCGGCT CGACCTGCGC GCCGCGGCCG	19320
	GTGCCACCGC TCTCCCGGAG GTCCTCGGTG ACCTGGCCCG CGTACCGCGG GACGCCCCGA	19380
15	GCACGCCCCG GGCCGCGGCG GGCACCGGGG ACGAGGACGG TGCCGTGCGC CCTGCCCCCG	19440
	CCCCGGCCGA CGCCGCGGGG ACGCTGGCCG CGCGGCTCGC GGGACGTTCC GCACCCGAGC	19500
	GTACGGCTCT CCTGCTCGAC CTGGTCCGGA CCGAGGTGCG GCGGTGCTC GGACACGGCG	19560
20	ACCCCGCCGC GATCGGCGCC GCCCGACCT TCAAGGACGC CGGATTCGAC TCCCTCACCG	19620
	CTGTGACCT CCGCAACCG CTGAACACAC GCACCGGACT GCGGCTGCCC GCGACCTCG	19680
25	TCTTCGACCA CCCCACACCG CTCGCCCTCG CCGAACTCCT GCTCGACGGG CTGGAGGCGG	19740
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30	TCCGCGCGGC ACGGCGGCTG CGCGGCCTGC TGGACGCGCT CCCC GCCGT CCCGGTGCCG	19920
	CGTCCGGTCC GGATGCCGGA GAGCACGCC CCGGTGCGG CGACGTGGTG ATCGACCGGC	19980
	TCAGGTCCGC CTCGACGAC GACTTGTTG ACCTGCTCGA CAGCGACTTC CAGTGAGCCG	20040
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40	ATCGCGATCG TGGGCATGGC GTGCCGTTAC CCGGCGGTG TGGCGTCGCC GGAGGAGCTG	20280
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	GTCATGTACC ACGACTACGG CAGCCACCAG GTCGGCACCG CCGCCGATCC CAGTGGACAG	20640
	CTCGGCCCTG GCACCGCGGG GAGCGTCGCC TCGGGCCGG TGGCGTACAC CCTCGGTCTA	20700
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	CGGTGCAAGG CGTTGCGGGA GGGCGCCGAC GGCACGGCGT GGGCCGAGGG CGCCGGTGTG	20940
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	GCCAGCAGC GGGTGATCCG TGACGCGCTG GCCGACGCGG GGCTGACGCC CGCCGACGTG	21120
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	CTGATGGCCA CCTACGGCAG TGAACGGGTG GGCGACCCGC TGTGGCTGGG TTCGCTGAAG	21240
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	GAATGGGACG CGGGCGCCGT GCAACTGCTC ACCGGCGTCC GGCCATGGCC CCGGCGCGAG	21420
	CACAGGCCCC GGGGGGCCGC GGTCTCCGCC TTCGGCGTCA GCGGCACCAA CGCCCACGTC	21480
25	ATCATCGAGG AACC GCCCGC GGGCGGTGAC ACCTCGCCCG CCGGCGACAC CCCTGAGCCG	21540
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30	GCCCTGCGCG CCCAGGCCGC CCGCCTGCGG GCGCACCTCG AACGCCTCCC CGGCACCTCG	21720
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35	CTGCTCGGCG ACGACGGAGC CCGGTTCGAC GCACTCGCCG CCCTCGCCGC CGGCGAGACC	21840
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	GCCACCTTCG CCGTCATGGT GGGACTCGCC GCGCTGTGGC GCTCCCTCGG GGTGGAACCC	22140
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	CCCGGCGCCC TGGAGGCGTT GCTCGTCACG CTGGAGAGCG AAGGCACCCG GGTCCGCCGC	22440
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	GCACGCACCG	GACGCGCCGA	GCTGTTCCGC	CTGCTCGAGA	CGGAGATCAA	CGGCGACACC	23220
25	GCCGTACCG	GCGTCGTCTC	GCTGCTCGGA	CTGTGCACCG	ACGGCAGGCC	GGACCACCCC	23280
	GCCGTGCCCC	TCGCCGTAC	CGCCACCCTC	GCCCTCGTCC	AGGCCCTGGC	CGACCTCGGC	23340
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35	GTCTTCGGCC	GCCGGGTCC	GCGGAACCCG	GCCGACTCCC	GGCCCCCGGC	CTGGCGCGCC	23640
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45	CTGGTGCCCC	TGGCGCCGCT	GCGGGAGACG	GCACCCGGCG	ACATCGCCGC	CGCCCTCGCC	23940
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	TTCTCAGCC	GGCGCGGGCT	GGCTCCCTC	GACCCCGACC	AGGCGGTGCG	GACCTGCGC	24240
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	GCCGCCTCCT	ACACCTGGGT	GCGTCCCCGC	GTACTCTTCG	ACGACATCCC	GGACGTGCAG	24360	
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	GCCCGGCACC	TCGGTGAGGA	ACTCTTCGGC	CGGAACGACA	CGCCGACCG	GGCCGGCCCC	24720	
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35	GACTACGCCC	TCGCCGGCGG	GGCCACGGTG	ATGTCCACCC	CCGAGATGCT	GGTGAGTTC	25380	
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	GCGCGGCGCC	TGCGCGCCGA	CCTGCTCGCC	CACCCCGAGC	TGCACCCGGC	CGACGTCCGC	26220
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10	TTACACGGAGC	TGATCGCGGC	CCTCGACGAC	CTCGTCGAAG	GCCGACCGCA	CCCGCTCGTG	26340
	CTGCGGGGCA	CCGCCGGCAC	CTCCGACCAG	GTCGTGTTTC	TCTTCCCCCG	CCAGGGCTCG	26400
	CAGTGGCCCC	AGATGGCCGA	CGGGCTGCTG	GCCCGCTCCA	GCGGCTCCGG	CTCCTTCCTG	26460
15	GAGACCGCCC	GCGCCTGCGA	CCTCGCGCTC	CGGCCCCACC	TCGGCTGGTC	CGTCCTGGAC	26520
	GTA CTGCGCC	GGGAACCCGG	CGCGCCCTCG	CTCGACCGGG	TCGACGTGGT	GCAGCCCGTG	26580
	CTGTTCACCA	TGATGGTCTC	GCTCGCCGAG	ACGTGGCGTT	CGCTGGGCGT	CGAACCGGCC	26640
20	GCGGTCTGTC	GTCAC TCCCA	GGGCGAGATC	GCCGCGCCT	ACGTGCGCCG	CGCCCTGACG	26700
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25	AAGGGCGGCA	TGGTCGCCGT	GACCCTGTCC	GAACGCGACC	TGCGTCCCCG	CCTGGAGCCC	26820
	TGGAGCGACC	GGCTCGCCGT	CGCGGCCGTC	AACGGCCCCG	AGACCTGCGC	CGTCTCCGGG	26880
	GACCCGGACG	CCCTGGCGGA	GCTGGTCGCC	GAAC TCGGTG	CGGAGGGCGT	GCAGCCCGC	26940
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40	CTGGGCGTCG	CCCTCTGCCG	CGCCTACACC	CACGGCCTGG	AGATCGACGC	CGAGGCCATC	27360
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	CTGCGGTGA	ACGTGCGGCG	CCCGGCACC	GACGACGCC	GCCGCTTCGC	CGTGACGCC	27780
55	CGCGCCGAGG	GCGCCACGGA	CTGGACCCCTG	CACGCCGAGG	GGCTGCTCAC	CGCGCAGGAC	27840

	ACGGCCGACG	CGCCGGACGC	CTCGGCGGCC	ACCCGCCCCC	CGGGCGCCGA	ACAACTGGAC	27900
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	GGACTGGTGA	GCGCCCACCG	CTGCGGCCCC	GACATCCACG	CGGAGGTCCG	GCTGCCCCGC	28020
	CAGGCGCAGG	GCGACGCGGC	CCGCTTCGGC	ATCCATCCCG	CGCTGCTGGA	CGCGGCGCTG	28080
10	CAGACCATGA	GCCTCGGGGG	CTTCTTCCCC	GAGGACGGCC	GCGTCCGCAT	GCCGTTCCGC	28140
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15	GTCTCCGAGG	ACGCGGTCCG	CATCAGGTGC	GCCGACGGCG	AGGGACGGCC	GGTCGCCGAG	28260
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	GCGCCGACG	CGCTCTTCCG	CATCGCCTGG	CGGAACTCG	CCGCCGGCCC	GGGCACCCGT	28380
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	CTGGCCGAGG	CGGCCGACGC	CCACCTGCCC	GCCGTTCCCG	GCCCCGACGG	CGCACTGCCG	28500
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25	GACGTCGCCC	CCGACGCGCA	CACCGTGGCC	TGCCGGGTGC	TGGACCTCGT	CCAGCGCCGG	28620
	CTCGCGGCCC	CGGAGGGCCC	GGACGGCGCC	CGCTGGTGG	TGGCCACCCG	CGGCGCGGTC	28680
	GCCGTACGCG	ACGACGCCGA	GGTGGACGAC	CCGGCCGCGG	CCGCCGCGTG	GGGCCTGCTG	28740
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35	GCCGGGACGG	TGTACGTGCC	CCGGTGGAG	CGGGCCGCCG	ACCGCACGGA	CGGGCCGCTC	28920
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	ACCGGTGTGC	CCGTCCGCGA	CCGCTGCTC	GGCCTGTGGG	ACGGCGGCCT	GGGCCCGCTG	29220
45	TGCGTGGCCG	ACCACCGGCT	GCTCGCCCCC	GTCCCGGACG	GCTGGTCCTA	CGCCCAGGCC	29280
	GCCTCGGTCC	CCGCGGTGTT	CCTCAGCGCC	TACTACGGTC	TGGTCACCCCT	GGCCGGCCTC	29340
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	GCCCTGCGCG	CCATGGGCAT	CACCGACGAC	CACCTCGCCT	CCTCCCGCAC	CCTCGACTTC	29520
55	GCGACCGCCT	TCACCGGAGC	GGACGGCACG	TCCCGCGCGG	ACGTGCTCCT	GAACTCGCTC	29580



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	TACCGGGCGT TCGACCTCAA CGAGGCCGGA CCCGACGCAC TCGGCCGGCT GCTGCGGGAA	29760
	CTGATGGACC TGTTCGCCGC CGGCGTGCTG CACCCGCTGC CCGTCGTAC CCACGACGTG	29820
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	CGAGGACGCC CGGGTCGACG CCGGGCCCCC CTTCGGGAC CTCGGCTTCG ACTCGCTCGC	40800
20	CGCGGTGCGG CTGCGCCGCC GGCTGGCCGA GGACACCGGG CTCGACCTGC CCGGCACCTT	40860
	CGTCTTCGAC CACGAGGACC CCACCGCGCT GGCCCCACCAC CTGGCCGGCC TCGCCGACGC	40920
25	GGGACCCCC GCGCCCCAGG AGGGCACGGC TCGGGCCGAG AGCGGGCTGT TCGCCTCCTT	40980
	CCGCGCCGCC GTCGAACAGC GCAGGTCGAG CGAGGTCGTG GAGCTGATGG CCGACCTGGC	41040
	GGGTTCCGG CCCGCCACT CCCGCGAGCA CCGCGCTCC GGCCGCCCCG CGCCCGTACC	41100
30	CCTCGCGACC GGACCGGCGA CGGTCCCAC GCTGTACTGC TCGCGCCGCA CCGCGTCCG	41160
	CTCCGGCCCC GCGGAGTACG TCCCGTTGCG CGAAGGACTG CCGGGCGTCC GGGAGACGGT	41220
	CGCCCTTCCC CTGTCCGGCT TCGGCGACCC CGCGGAACCG ATGCCCCGAT CGCTCGACGC	41280
35	GCTGATCGAG GTCCAGGCCG ACGTCTCCT GGAGCACACC GCGGGCAAGC CCTTCGCCCT	41340
	CGCCGGCCAC TCCGCCGGCG CGAACATCGC CCACGCCCTG GCGCCCCGGC TGGAGGAACG	41400
40	CGGCTCGGGC CCGCGAGCCG TCGTACTGAT GGACGTCTAC CGTCCCGAGG ACCCGGTGC	41460
	GATGGGCGAG TGGCCGACG ACCTGCTCAG CTGGGCGCTC GAACGCAGCA CCGTGCCCTT	41520
	GGAGGACCAC CGGCTCACC GATGCGCCG CTATCAGCG CTGGTGCTCG GAACCCGGCT	41580
45	CACCGCCCTC GAAGCCCCCG TCCTGCTGGC CCGGGCGTCC GAACCCCTGT GCGCGTGGCC	41640
	GCCCGCGGGC GGGGCGCGG GCGACTGGCG GTCCAGGTC CCGTTCGCAC GGACCGTCGC	41700
	CGACGTGCCC GGCAACCACT TCACCATGCT CACCGAACAC GCGCGGCACA CCGCGTCCCT	41760
50	GGTGACGAA TGGCTGGACA GCCTCCCGCA CCAGCCCGT CCGCCCCGC TCACCGGAGG	41820
	GAAACACTGA TGTACGCCGA CGACATCGCG GCCGTCTACG ACCTGGTCCA CGAGGGGAAG	41880
	GGGAAGGACT ACCGGCAGGA GGCCGAGGAG ATCGCCGCAC TCGTGCGGT CCACCGGCCG	41940
55	GGCGCCCGGA CCCTGCTCGA CGTGGCCTGC GGCACCGGC AGCACCTGCA CCACCTGGAC	42000

	GGCCTCTTCG ACCACGTCGA GGGCCTGGAA CTCTCCGCCG ACATGCTGGC CCTCGCGACC	42060
5	GGCCGGAACC CCGGTGTAC CTTCCACCAA GGGACATGC GCTCGTTCTC CCTGGGACGC	42120
	CGGTTCGACG CCGTGACCTG CATGTTTCAGC TCCATAGGCC ACCTGCGGAC CACCGACGAA	42180
	CTCGACAGCA CGCTGCGGGC CTTACCGAC CACCTCGAAC CGTCCGGCGT CATCGTCGTC	42240
10	GAACCTTGGT GGTTCCTCCGA GTCTTCACCC CCCGTTACG TCGGCGCCAG CATCACGGAG	42300
	GCGGGCGAGC GCACCGTCTG CCGGTCTCTG CACTCCGTAC GGGAGGGGAA CGCCACCCGC	42360
15	ATCGAGGTGC ACTACCTCCT CGCCGACCC GCGGCGCTCC GTCACCTGAC CGAGGACCAC	42420
	ACCATCACCC TGTTCCCGCG CGCCGACTAC GAGGCGGCCT TCGAGCGCGC CGGCTCGAC	42480
	GTGGTCTACC AGGAAGGCGG CCCGTCCGGT CCGGGCTGT TCATCGGCAC CCGCGCTGA	42540
20	CCCGGTGCCG ACGCGGACCG CCGCGGCCCG GAGGCGGGTT GCCCCGACCC ACCCGGCACA	42600
	CCCGGGTCCC CCGATCGTGC GAGCGCCCC ATCGACCCGA GAAGAAAGGC AGGGCAGCCA	42660
	TGCCCCACCT TGCCACGAA ACGGCCCCG CGACACGAG CACGAGCGCG GGCACGAGCA	42720
25	CGGGCGTCCG TGCGCTCGGC CGTCGGCTCC AGCTGACCCG GGCCGCACAC TGGTGGCCCG	42780
	GCAACCAGGG CGACCCGTAC GCGCTGATCC TGCGCGCCGT CGCCGACCC GAGCGTTTCG	42840
	AACGGGAGAT CCGGGCCCGC GGACCGTGGT TCCGCAGCGA ACAGCTGGAC GCCTGGGTGA	42900
30	CCGCGGACCC CGAGGTGGCG GCGGCCGTCC TGGCCGACCC GCGCTTCGGC ACGCTGGACC	42960
	GGGCCGGACG CCGCCCGAC GAGGAACTGC TGCCCCTCGC CGAGGCGTTC CCCCACCACG	43020
35	AACGCGCGGA GCTCGTACGC CTGCGGGCGC TGGCCGCCCC GGTGCTCAGC CGGTACGCCC	43080
	CGGCCCAGGC GCCCTGCGCG GCGCGACCA CCGCCGCGAG AGTGCTCGGC CGCCTGCTGC	43140
	CCACCGGTGA CGCCGGGTTC GACCTTGTCG GCGAGGTGCG CCGGCCCTAC GCCGTGAGC	43200
40	TGATGCTCAG GCTCCTCGGA GTGCCGGGCC GCGACCGCGC CACCGCCGCG CGGGCACTCG	43260
	CCGCCTGCGG CCCCAGCTC GACGCCCGGA TGGCCCCGCA ACTGCTGACC GTGGCCCGGG	43320
	AGTCCGCCGA CGCCGTCCGC AACTGGCCG ACCTGGTCCC CGAGCTCGTC GCGGAGAAGT	43380
45	CCCGGGGCTT CCGGAACGCC GAGCCCCGGC CCGACGACGT GCTCGCCCTC CTCCTGCACG	43440
	ACGGCGTCGC CCCCAGCGAC GTCGAGCGCA TCGCGCTGCT CCTCGCGGTC GGCGCACCCG	43500
50	AACCCGTCTG CACCGCCGTC GCGCACACGG TCCACCGGCT GCTCGGCCGG CCGGGGAGT	43560
	GGGAGAGGGC CCGCCGAGC CCGCCCGCG CGAACGCCGT CGACCAGGTG CTCGCGGAGC	43620
	GCCCCCGGC CCGCTGGAG AACCGGGTCG CGCACACCG CCTCGAACTC GCGGCGCGCC	43680
55	GGATCACCGC CGACGAGCAC GTCGTGGTGC TGGCCGCCGC CGGACGGGAG ATCCCCGGGC	43740



CGGAGCCGCT CGGGGGCGCC GACGGACCGC ACCTGGCGCT CGCCCTCCCG CTGATCCGCC 43800  
 5 TGGCCGCCAC CACCGCGGTC CAGGTCACGG CCGGCCGCTT GCGCGGCTTG CGGGCCGAGG 43860  
 GACCGCCCTT GACCGGCGCG CGGTCACCGG TCCTGGGCGC CTGCGCCCGC CTCCGGGTCC 43920  
 ACCCGGGATG ACCCGCCCGT CCGTACGCCC CCTCCAGAC CGGAGCCGCT GTGCGCGTCC 43980  
 10 TGCTGACATC CCTCGCCAC AACACCCACT ACTACAGTCT GGTGCCCCCTC GCCTGGGCGC 44040  
 TGGCGCCCGC CGGGCACGAG GTACGGGTGG CGAGCCCGCC CTCCCTCACC GACGTCATCA 44100  
 CCTCCACCGG TCTGACCGCC GTACCGGTGG GCGACGACCG ACCGGCCGCG GAGCTGCTCG 44160  
 15 CCGAGATGGG CAGAGACCTC GTCCCCTACC AGAGGGGCTT CGAGTTCGGT GAGGTGGAGA 44220  
 JGCGAGGAGGA GACCACCTGG GAGTACCTGC TCGGCCAGCA GAGCATGATG GCCGCCCTGT 44280  
 GCTTCGCCCC GTTCAACGGC GCCGCCACGA TGGACGAGAT CGTCGACTTC GCCCGTGGCT 44340  
 20 GGCGGCCCCGA CCTGGTCGTG TGGGAACCCT GGACCTA 44377

## (2) INFORMATION FOR SEQ ID NO:2:

25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 4550 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: unknown

30 (ii) MOLECULE TYPE: peptide

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

35 Met Ser Gly Glu Leu Ala Ile Ser Arg Ser Asp Asp Arg Ser Asp Ala  
 1 5 10 15  
 Val Ala Val Val Gly Met Ala Cys Arg Phe Pro Gly Ala Pro Gly Ile  
 20 25 30  
 40 Ala Glu Phe Trp Lys Leu Leu Thr Asp Gly Arg Asp Ala Ile Gly Arg  
 35 40 45  
 Asp Ala Asp Gly Arg Arg Arg Gly Met Ile Glu Ala Pro Gly Asp Phe  
 50 55 60  
 45 Asp Ala Ala Phe Phe Gly Met Ser Pro Arg Glu Ala Ala Glu Thr Asp  
 65 70 75 80  
 Pro Gln Gln Arg Leu Met Leu Glu Leu Gly Trp Glu Ala Leu Glu Asp  
 85 90 95  
 50 Ala Gly Ile Val Pro Gly Ser Leu Arg Gly Glu Ala Val Gly Val Phe  
 100 105 110  
 55 Val Gly Ala Met His Asp Asp Tyr Ala Thr Leu Leu His Arg Ala Gly  
 115 120 125

Ala Pro Val Gly Pro His Thr Ala Thr Gly Leu Gln Arg Ala Met Leu  
 130 135 140  
 5 Ala Asn Arg Leu Ser Tyr Val Leu Gly Thr Arg Gly Pro Ser Leu Ala  
 145 150 155 160  
 Val Asp Thr Ala Gln Ser Ser Ser Leu Val Ala Val Ala Leu Ala Val  
 165 170 175  
 10 Glu Ser Leu Arg Ala Gly Thr Ser Arg Val Ala Val Ala Gly Gly Val  
 180 185 190  
 Asn Leu Val Leu Ala Asp Glu Gly Thr Ala Ala Met Glu Arg Leu Gly  
 195 200 205  
 15 Ala Leu Ser Pro Asp Gly Arg Cys His Thr Phe Asp Ala Arg Ala Asn  
 210 215 220  
 Gly Tyr Val Arg Gly Glu Gly Gly Ala Ala Val Val Leu Lys Pro Leu  
 225 230 235 240  
 20 Ala Asp Ala Leu Ala Asp Gly Asp Pro Val Tyr Cys Val Val Arg Gly  
 245 250 255  
 Val Ala Val Gly Asn Asp Gly Gly Gly Pro Gly Leu Thr Ala Pro Asp  
 260 265 270  
 25 Arg Glu Gly Gln Glu Ala Val Leu Arg Ala Ala Cys Ala Gln Ala Arg  
 275 280 285  
 Val Asp Pro Ala Glu Val Arg Phe Val Glu Leu His Gly Thr Gly Thr  
 290 295 300  
 30 Pro Val Gly Asp Pro Val Glu Ala His Ala Leu Gly Ala Val His Gly  
 305 310 315 320  
 35 Ser Gly Arg Pro Ala Asp Asp Pro Leu Leu Val Gly Ser Val Lys Thr  
 325 330 335  
 Asn Ile Gly His Leu Glu Gly Ala Ala Gly Ile Ala Gly Leu Val Lys  
 340 345 350  
 40 Ala Ala Leu Cys Leu Arg Glu Arg Thr Leu Pro Gly Ser Leu Asn Phe  
 355 360 365  
 Ala Thr Pro Ser Pro Ala Ile Pro Leu Asp Gln Leu Arg Leu Lys Val  
 370 375 380  
 45 Gln Thr Ala Ala Ala Glu Leu Pro Leu Ala Pro Gly Gly Ala Pro Leu  
 385 390 395 400  
 Leu Ala Gly Val Ser Ser Phe Gly Ile Gly Gly Thr Asn Cys His Val  
 405 410 415  
 50 Val Leu Glu His Leu Pro Ser Arg Pro Thr Pro Ala Val Ser Val Ala  
 420 425 430  
 55 Ala Ser Leu Pro Asp Val Pro Pro Leu Leu Leu Ser Ala Arg Ser Glu  
 435 440 445

Gly Ala Leu Arg Ala Gln Ala Val Arg Leu Gly Glu Tyr Val Glu Arg  
 450 455 460  
 5 Val Gly Ala Asp Pro Arg Asp Val Ala Tyr Ser Leu Ala Ser Thr Arg  
 465 470 475 480  
 Thr Leu Phe Glu His Arg Ala Val Val Pro Cys Gly Gly Arg Gly Glu  
 485 490 495  
 10 Leu Val Ala Ala Leu Gly Gly Phe Ala Ala Gly Arg Val Ser Gly Gly  
 500 505 510  
 Val Arg Ser Gly Arg Ala Val Pro Gly Gly Val Gly Val Leu Phe Thr  
 515 520 525  
 15 Gly Gln Gly Ala Gln Trp Val Gly Met Gly Arg Gly Leu Tyr Ala Gly  
 530 535 540  
 Gly Gly Val Phe Ala Glu Val Leu Asp Glu Val Leu Ser Met Val Gly  
 545 550 555 560  
 20 Glu Val Asp Gly Arg Ser Leu Arg Asp Val Met Phe Gly Asp Val Asp  
 565 570 575  
 Val Asp Ala Gly Ala Gly Ala Asp Ala Gly Ala Gly Ala Gly Ala Gly  
 580 585 590  
 25 Val Gly Ser Gly Ser Gly Ser Val Gly Gly Leu Leu Gly Arg Thr Glu  
 595 600 605  
 Phe Ala Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu Phe Arg Ala  
 610 615 620  
 30 Leu Glu Ala Arg Gly Val Glu Val Ser Val Val Leu Gly His Ser Val  
 625 630 635 640  
 Gly Glu Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser Leu Gly Asp  
 645 650 655  
 35 Ala Val Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly Gly Leu Pro  
 660 665 670  
 Val Gly Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser Val Val Arg  
 675 680 685  
 Gly Val Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala Ala Val Asn  
 690 695 700  
 45 Gly Pro Arg Ser Val Val Leu Ser Gly Asp Val Gly Val Leu Glu Ser  
 705 710 715 720  
 Val Val Ala Ser Leu Met Gly Asp Gly Val Glu Cys Arg Arg Leu Asp  
 725 730 735  
 50 Val Ser His Gly Phe His Ser Val Leu Met Glu Pro Val Leu Gly Glu  
 740 745 750  
 Phe Arg Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val Arg Pro Gly  
 755 760 765  
 55

Val Val Val Val Ser Gly Val Ser Gly Gly Val Val Gly Ser Gly Glu  
 770 775 780  
 5 Leu Gly Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu Ala Val Arg  
 785 790 795 800  
 Phe Ala Asp Gly Val Gly Val Val Arg Gly Leu Gly Val Gly Thr Leu  
 805 810 815  
 10 Val Glu Val Gly Pro His Gly Val Leu Thr Gly Met Ala Gly Glu Cys  
 820 825 830  
 Leu Gly Ala Gly Asp Asp Val Val Val Val Pro Ala Met Arg Arg Gly  
 835 840 845  
 15 Arg Ala Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr Val Phe Thr  
 850 855 860  
 Arg Asp Ala Gly Leu Asp Ala Thr Ala Leu His Thr Gly Ser Thr Gly  
 865 870 875 880  
 20 Arg Arg Ile Asp Leu Pro Thr Tyr Pro Phe Gln Arg Arg Thr His Trp  
 885 890 895  
 Ser Pro Ala Leu Ser Arg Pro Val Thr Ala Asp Ala Gly Ala Gly Val  
 900 905 910  
 25 Thr Ala Thr Asp Ala Val Gly His Ser Val Ser Pro Asp Pro Glu Ser  
 915 920 925  
 Thr Glu Gly Thr Ser His Arg Asp Thr Asp Asp Glu Ala Asp Ser Ala  
 930 935 940  
 30 Ser Pro Glu Pro Met Ser Pro Glu Asp Ala Val Arg Leu Val Arg Glu  
 945 950 955 960  
 Ser Thr Ala Ala Val Leu Gly His Asp Asp Pro Gly Glu Val Ala Leu  
 965 970 975  
 Asp Arg Thr Phe Thr Ser Gln Gly Met Asp Ser Val Thr Ala Val Glu  
 980 985 990  
 40 Leu Cys Asp Leu Leu Lys Gly Ala Ser Gly Leu Pro Leu Ala Ala Thr  
 995 1000 1005  
 Leu Val Tyr Asp Leu Pro Thr Pro Arg Ala Val Ala Glu His Ile Val  
 1010 1015 1020  
 45 Glu Ala Ala Gly Gly Pro Lys Asp Ser Val Ala Gly Gly Pro Gly Val  
 1025 1030 1035 1040  
 Leu Ser Ser Ala Ala Val Gly Val Ser Asp Ala Arg Gly Gly Ser Arg  
 1045 1050 1055  
 50 Asp Asp Asp Asp Pro Ile Ala Ile Val Gly Val Gly Cys Arg Leu Pro  
 1060 1065 1070  
 Gly Gly Val Asp Ser Arg Ala Ala Leu Trp Glu Leu Leu Glu Ser Gly  
 1075 1080 1085  
 55

Ala Asp Ala Ile Ser Ser Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp  
 1090 1095 1100  
 5 Gly Leu Tyr Asp Pro Glu Pro Gly Thr Pro Gly Lys Thr Tyr Val Arg  
 1105 1110 1115 1120  
 Glu Gly Gly Phe Leu His Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe  
 1125 1130 1135  
 10 Gly Ile Ser Pro Arg Glu Ala Thr Ala Met Asp Pro Gln Gln Arg Leu  
 1140 1145 1150  
 Leu Leu Glu Ala Ser Trp Glu Ala Leu Glu Asp Ala Gly Val Leu Pro  
 1155 1160 1165  
 15 Glu Ser Leu Arg Gly Gly Asp Ala Gly Val Phe Val Gly Ala Thr Ala  
 1170 1175 1180  
 Pro Glu Tyr Gly Pro Arg Leu His Glu Gly Ala Asp Gly Tyr Glu Gly  
 1185 1190 1195 1200  
 20 Tyr Leu Leu Thr Gly Thr Thr Ala Ser Val Ala Ser Gly Arg Ile Ala  
 1205 1210 1215  
 Tyr Thr Leu Gly Thr Gly Gly Pro Ala Leu Thr Val Asp Thr Ala Cys  
 1220 1225 1230  
 25 Ser Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ala Leu Arg Arg  
 1235 1240 1245  
 Gly Glu Cys Gly Leu Ala Leu Ala Gly Gly Ala Thr Val Met Ser Gly  
 1250 1255 1260  
 30 Pro Gly Met Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Pro Asp  
 1265 1270 1275 1280  
 Gly Arg Cys Met Pro Phe Ser Ala Asp Ala Asp Gly Thr Ala Trp Ser  
 1285 1290 1295  
 35 Glu Gly Val Ala Val Leu Ala Leu Glu Arg Leu Ser Asp Ala Arg Arg  
 1300 1305 1310  
 Ala Gly His Arg Val Leu Gly Val Val Arg Gly Ser Ala Val Asn Gln  
 1315 1320 1325  
 Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Arg Ser Ala Gln Glu  
 1330 1335 1340  
 45 Gly Val Ile Arg Ala Ala Leu Ala Asp Ala Gly Leu Ala Pro Gly Asp  
 1345 1350 1355 1360  
 Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Ala Leu Gly Asp Pro  
 1365 1370 1375  
 50 Ile Glu Ala Ser Ala Leu Leu Ala Thr Tyr Gly Arg Glu Arg Val Gly  
 1380 1385 1390  
 Asp Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Val Gly His Thr Gln  
 1395 1400 1405  
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5           Ala Ala Ala Gly Ala Ala Gly Val Val Lys Met Leu Leu Ala Leu Glu  
             1410                      1415                      1420  
 His Gly Thr Leu Pro Arg Thr Leu His Ala Asp Arg Pro Ser Thr His  
 1425                      1430                      1435                      1440  
 Val Asp Trp Ser Ser Gly Thr Val Ala Leu Leu Ala Glu Ala Arg Arg  
 10                      1445                      1450                      1455  
 Trp Pro Arg Arg Ser Asp Arg Pro Arg Arg Ala Ala Val Ser Ser Phe  
                     1460                      1465                      1470  
 Gly Ile Ser Gly Thr Asn Ala His Leu Ile Ile Glu Glu Ala Pro Glu  
 15                      1475                      1480                      1485  
 Trp Val Glu Asp Ile Asp Gly Val Ala Ala Pro Asp Arg Gly Thr Ala  
                     1490                      1495                      1500  
 Asp Ala Ala Ala Pro Ser Pro Leu Leu Leu Ser Ala Arg Ser Glu Gly  
 20                      1505                      1510                      1515                      1520  
 Ala Leu Arg Ala Gln Ala Val Arg Leu Gly Glu Tyr Val Glu Arg Val  
                     1525                      1530                      1535  
 Gly Ala Asp Pro Arg Asp Val Ala Tyr Ser Leu Ala Ser Thr Arg Thr  
 25                      1540                      1545                      1550  
 Leu Phe Glu His Arg Ala Val Val Pro Cys Gly Gly Arg Gly Glu Leu  
                     1555                      1560                      1565  
 Val Ala Ala Leu Gly Gly Phe Ala Ala Gly Arg Val Ser Gly Gly Val  
 30                      1570                      1575                      1580  
 Arg Ser Gly Arg Ala Val Pro Gly Gly Val Gly Val Leu Phe Thr Gly  
                     1585                      1590                      1595                      1600  
 Gln Gly Ala Gln Trp Val Gly Met Gly Arg Gly Leu Tyr Ala Gly Gly  
 35                      1605                      1610                      1615  
 Gly Val Phe Ala Glu Val Leu Asp Glu Val Leu Ser Met Val Gly Glu  
                     1620                      1625                      1630  
 Val Asp Gly Arg Ser Leu Arg Asp Val Met Phe Gly Asp Val Asp Val  
 40                      1635                      1640                      1645  
 Asp Ala Gly Ala Gly Ala Asp Ala Gly Ala Gly Ala Gly Ala Gly Val  
                     1650                      1655                      1660  
 Gly Ser Gly Ser Gly Ser Val Gly Gly Leu Leu Gly Arg Thr Glu Phe  
 45                      1665                      1670                      1675                      1680  
 Ala Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu Phe Arg Ala Leu  
                     1685                      1690                      1695  
 Glu Ala Arg Gly Val Glu Val Ser Val Val Leu Gly His Ser Val Gly  
                     1700                      1705                      1710  
 Glu Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser Leu Gly Asp Ala  
 55                      1715                      1720                      1725

Val Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly Gly Leu Pro Val  
 1730 1735 1740  
 5 Gly Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser Val Val Arg Gly  
 1745 1750 1755 1760  
 Val Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala Ala Val Asn Gly  
 1765 1770 1775  
 10 Pro Arg Ser Val Val Leu Ser Gly Asp Val Gly Val Leu Glu Ser Val  
 1780 1785 1790  
 Val Ala Ser Leu Met Gly Asp Gly Val Glu Cys Arg Arg Leu Asp Val  
 1795 1800 1805  
 15 Ser His Gly Phe His Ser Val Leu Met Glu Pro Val Leu Gly Glu Phe  
 1810 1815 1820  
 Arg Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val Arg Pro Gly Val  
 1825 1830 1835 1840  
 20 Val Val Val Ser Gly Val Ser Gly Gly Val Val Gly Ser Gly Glu Leu  
 1845 1850 1855  
 Gly Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu Ala Val Arg Phe  
 1860 1865 1870  
 25 Ala Asp Gly Val Gly Val Val Arg Gly Leu Gly Val Gly Thr Leu Val  
 1875 1880 1885  
 Glu Val Gly Pro His Gly Val Leu Thr Gly Met Ala Gly Glu Cys Leu  
 1890 1895 1900  
 Gly Ala Gly Asp Asp Val Val Val Val Pro Ala Met Arg Arg Gly Arg  
 1905 1910 1915 1920  
 30 Ala Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr Val Phe Thr Arg  
 1925 1930 1935  
 Asp Ala Gly Leu Asp Ala Thr Ala Leu His Thr Gly Ser Thr Gly Arg  
 1940 1945 1950  
 40 Arg Ile Asp Leu Pro Thr Tyr Pro Phe Gln Arg Asp Arg Tyr Trp Leu  
 1955 1960 1965  
 Asp Pro Val Arg Thr Ala Val Thr Gly Val Glu Pro Ala Gly Ser Pro  
 1970 1975 1980  
 45 Ala Asp Ala Arg Ala Thr Glu Arg Gly Arg Ser Thr Thr Ala Gly Ile  
 1985 1990 1995 2000  
 Arg Tyr Arg Val Ala Trp Gln Pro Ala Val Val Asp Arg Gly Asn Pro  
 2005 2010 2015  
 50 Gly Pro Ala Gly His Val Leu Leu Leu Ala Pro Asp Glu Asp Thr Ala  
 2020 2025 2030  
 Asp Ser Gly Leu Ala Pro Ala Ile Ala Arg Glu Leu Ala Val Arg Gly  
 2035 2040 2045  
 55

Ala Glu Val His Thr Val Ala Val Pro Val Gly Thr Gly Arg Glu Ala  
 2050 2055 2060  
 5 Ala Gly Asp Leu Leu Arg Ala Ala Gly Asp Gly Ala Ala Arg Ser Thr  
 2065 2070 2075 2080  
 Arg Val Leu Trp Leu Ala Pro Ala Glu Pro Asp Ala Ala Asp Ala Val  
 2085 2090 2095  
 10 Ala Leu Val Gln Ala Leu Gly Glu Ala Val Pro Glu Ala Pro Leu Trp  
 2100 2105 2110  
 Ile Thr Thr Arg Glu Ala Ala Ala Val Arg Pro Asp Glu Thr Pro Ser  
 2115 2120 2125  
 15 Val Gly Gly Ala Gln Leu Trp Gly Leu Gly Gln Val Ala Ala Leu Glu  
 2130 2135 2140  
 Leu Gly Arg Arg Trp Gly Gly Leu Ala Asp Leu Pro Gly Ser Ala Ser  
 2145 2150 2155 2160  
 20 Pro Ala Val Leu Arg Thr Phe Val Gly Ala Leu Leu Ala Gly Gly Glu  
 2165 2170 2175  
 Asn Gln Phe Ala Val Arg Pro Ser Gly Val His Val Arg Arg Val Val  
 2180 2185 2190  
 25 Pro Ala Pro Val Pro Val Pro Ala Ser Ala Arg Thr Val Thr Thr Ala  
 2195 2200 2205  
 30 Pro Ala Thr Ala Val Gly Glu Asp Ala Arg Asn Asp Thr Ser Asp Val  
 2210 2215 2220  
 Val Val Pro Asp Asp Arg Trp Ser Ser Gly Thr Val Leu Ile Thr Gly  
 2225 2230 2235 2240  
 35 Gly Thr Gly Ala Leu Gly Ala Gln Val Ala Arg Arg Leu Ala Arg Ser  
 2245 2250 2255  
 Gly Ala Ala Arg Leu Leu Leu Val Gly Arg Arg Gly Ala Ala Gly Pro  
 2260 2265 2270  
 40 Gly Val Gly Glu Leu Val Glu Glu Leu Thr Ala Leu Gly Ser Glu Val  
 2275 2280 2285  
 Ala Val Glu Ala Cys Asp Val Ala Asp Arg Asp Ala Leu Ala Ala Leu  
 2290 2295 2300  
 45 Leu Ala Gly Leu Pro Glu Glu Arg Pro Leu Val Ala Val Leu His Ala  
 2305 2310 2315 2320  
 Ala Gly Val Leu Asp Asp Gly Val Leu Asp Ser Leu Thr Ser Asp Arg  
 2325 2330 2335  
 50 Val Asp Ala Val Leu Arg Asp Lys Val Thr Ala Ala Arg His Leu Asp  
 2340 2345 2350  
 Glu Leu Thr Ala Asp Leu Pro Leu Asp Ala Phe Val Leu Phe Ser Ser  
 2355 2360 2365  
 55



Ile Val Gly Val Trp Gly Asn Gly Gly Gln Ala Val Tyr Ala Ala Ala  
 2370 2375 2380

5 Asn Ala Ala Leu Asp Ala Leu Ala Gln Arg Arg Arg Ala Arg Gly Ala  
 2385 2390 2395 2400

Arg Ala Ala Ser Ile Ala Trp Gly Pro Trp Ala Gly Ala Gly Met Ala  
 2405 2410 2415

10 Ser Gly Thr Ala Ala Lys Ser Phe Glu Arg Asp Gly Val Thr Ala Leu  
 2420 2425 2430

Asp Pro Glu Arg Ala Leu Asp Val Leu Asp Asp Val Val Gly Ala Gly  
 2435 2440 2445

15 Gly Thr Ser Ala Ala Gly Thr His Ala Ala Gly Glu Ser Ser Leu Leu  
 2450 2455 2460

Val Ala Asp Val Asp Trp Glu Thr Phe Val Gly Arg Ser Val Thr Arg  
 2465 2470 2475 2480

Arg Thr Trp Ser Leu Phe Asp Gly Val Ser Ala Ala Arg Ser Ala Arg  
 2485 2490 2495

25 Ala Gly His Ala Ala Asp Asp Arg Ala Ala Leu Thr Pro Gly Thr Arg  
 2500 2505 2510

Pro Gly Asp Gly Ala Pro Gly Gly Ser Gly Gln Asp Gly Gly Glu Gly  
 2515 2520 2525

30 Arg Pro Trp Leu Ser Val Gly Pro Ser Pro Ala Glu Arg Arg Arg Ala  
 2530 2535 2540

Leu Leu Thr Leu Val Arg Ser Glu Ala Ala Gly Ile Leu Arg His Ala  
 2545 2550 2555 2560

35 Ser Ala Asp Ala Val Asp Pro Glu Leu Ala Phe Arg Ser Ala Gly Phe  
 2565 2570 2575

Asp Ser Leu Thr Val Leu Glu Leu Arg Asn Arg Leu Thr Ala Ala Thr  
 2580 2585 2590

40 Gly Leu Asn Leu Pro Asn Thr Leu Leu Phe Asp His Pro Thr Pro Leu  
 2595 2600 2605

Ser Leu Ala Ser His Leu His Asp Glu Leu Phe Gly Pro Asp Ser Glu  
 2610 2615 2620

45 Ala Glu Pro Ala Ala Ala Ala Pro Thr Pro Val Met Ala Asp Glu Arg  
 2625 2630 2635 2640

Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly Gly Val  
 2645 2650 2655

50 Ala Ser Pro Asp Asp Leu Trp Asp Leu Val Ala Gly Asp Gly His Thr  
 2660 2665 2670

55 Leu Ser Pro Phe Pro Ala Asp Arg Gly Trp Asp Val Glu Gly Leu Tyr  
 2675 2680 2685

Asp Pro Glu Pro Gly Val Pro Gly Lys Ser Tyr Val Arg Glu Gly Gly  
 2690 2695 2700  
 5 Phe Leu Arg Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe Gly Ile Ser  
 2705 2710 2715 2720  
 Pro Arg Glu Ala Thr Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu  
 2725 2730 2735  
 10 Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Val Pro Asp Ser Leu  
 2740 2745 2750  
 Arg Gly Thr Arg Thr Gly Val Phe Ser Gly Ile Ser Gln Gln Asp Tyr  
 2755 2760 2765  
 15 Ala Thr Gln Leu Gly Asp Ala Ala Asp Thr Tyr Gly Gly His Val Leu  
 2770 2775 2780  
 Thr Gly Thr Leu Gly Ser Val Ile Ser Gly Arg Val Ala Tyr Ala Leu  
 2785 2790 2795 2800  
 Gly Leu Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser Ser Ser  
 2805 2810 2815  
 20 Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly Glu Cys  
 2820 2825 2830  
 Asp Leu Ala Leu Ala Gly Gly Val Thr Val Met Ala Thr Pro Thr Val  
 2835 2840 2845  
 30 Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg Cys  
 2850 2855 2860  
 Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala Glu Gly Val  
 2865 2870 2875 2880  
 35 Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His  
 2885 2890 2895  
 Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala  
 2900 2905 2910  
 40 Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg Val Ile  
 2915 2920 2925  
 Arg Glu Ala Leu Ala Asp Ala Gly Leu Val Pro Ala Asp Val Asp Val  
 2930 2935 2940  
 45 Val Glu Ala His Gly Thr Gly Thr Ala Leu Gly Asp Pro Ile Glu Ala  
 2945 2950 2955 2960  
 Gly Ala Leu Leu Ala Thr Tyr Gly Arg Glu Arg Val Gly Asp Pro Leu  
 2965 2970 2975  
 50 Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala  
 2980 2985 2990  
 Gly Val Gly Gly Val Ile Lys Val Val Gln Gly Met Arg His Gly Ser  
 2995 3000 3005  
 55

Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ser Lys Val Glu Trp  
 3010 3015 3020

5 Ala Ser Gly Ala Val Glu Leu Leu Thr Glu Thr Arg Ser Trp Pro Arg  
 3025 3030 3035 3040

Arg Val Glu Arg Val Arg Arg Ala Ala Val Ser Ala Phe Gly Val Ser  
 3045 3050 3055

10 Gly Thr Asn Ala His Val Val Leu Glu Glu Ala Pro Ala Glu Ala Gly  
 3060 3065 3070

Ser Glu His Gly Asp Gly Pro Glu Pro Glu Arg Pro Asp Ala Val Thr  
 3075 3080 3085

15 Gly Pro Leu Ser Trp Val Leu Ser Ala Arg Ser Glu Gly Ala Leu Arg  
 3090 3095 3100

20 Ala Gln Ala Val Arg Leu Arg Glu Cys Val Glu Arg Val Gly Ala Asp  
 3105 3110 3115 3120

Pro Arg Asp Val Ala Gly Ser Leu Val Val Ser Arg Ala Ser Phe Gly  
 3125 3130 3135

25 Glu Arg Ala Val Val Val Gly Arg Gly Arg Glu Glu Leu Leu Ala Gly  
 3140 3145 3150

Leu Asp Val Val Ala Ala Gly Ala Pro Val Gly Val Ser Ser Gly Ala  
 3155 3160 3165

30 Gly Ala Val Val Arg Gly Ser Ala Val Arg Gly Arg Gly Val Gly Val  
 3170 3175 3180

Leu Phe Thr Gly Gln Gly Ala Gln Trp Val Gly Met Gly Arg Gly Leu  
 3185 3190 3195 3200

35 Tyr Ala Gly Gly Gly Val Phe Ala Glu Val Leu Asp Glu Val Leu Ser  
 3205 3210 3215

Val Val Gly Glu Val Asp Gly Arg Ser Leu Arg Asp Val Met Phe Ala  
 3220 3225 3230

40 Asp Ala Asp Ser Val Leu Gly Gly Leu Leu Gly Arg Thr Glu Phe Ala  
 3235 3240 3245

Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu Phe Arg Ala Leu Glu  
 3250 3255 3260

45 Ala Arg Gly Val Glu Val Ser Val Val Leu Gly His Ser Val Gly Glu  
 3265 3270 3275 3280

Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser Leu Gly Asp Ala Val  
 3285 3290 3295

Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly Gly Leu Pro Val Gly  
 3300 3305 3310

50 Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser Val Val Arg Gly Val  
 3315 3320 3325

55

Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala Ala Val Asn Gly Pro  
 3330 3335 3340  
 5 Arg Ser Val Val Leu Ser Gly Asp Val Gly Val Leu Glu Ser Val Val  
 3345 3350 3355 3360  
 Val Thr Leu Met Gly Asp Gly Val Glu Cys Arg Arg Leu Asp Val Ser  
 3365 3370 3375  
 10 His Gly Phe His Ser Val Leu Met Glu Pro Val Leu Gly Glu Phe Arg  
 3380 3385 3390  
 Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val Arg Pro Gly Val Val  
 3395 3400 3405  
 15 Val Val Ser Gly Val Ser Gly Gly Val Val Gly Ser Gly Glu Leu Gly  
 3410 3415 3420  
 Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu Ala Val Arg Phe Ala  
 3425 3430 3435 3440  
 20 Asp Gly Val Gly Val Val Arg Gly Leu Gly Val Gly Thr Leu Val Glu  
 3445 3450 3455  
 Val Gly Pro His Gly Val Leu Thr Gly Met Ala Gly Gln Cys Leu Glu  
 3460 3465 3470  
 25 Ala Gly Asp Asp Val Val Val Val Pro Ala Met Arg Arg Gly Arg Pro  
 3475 3480 3485  
 Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr Val Phe Thr Arg Asp  
 3490 3495 3500  
 Ala Gly Leu Asp Ala Thr Thr Leu His Thr Gly Ser Thr Gly Arg Arg  
 3505 3510 3515 3520  
 35 Ile Asp Leu Pro Thr Tyr Pro Phe Gln His Asn Arg Tyr Trp Ala Thr  
 3525 3530 3535  
 Gly Ser Val Thr Gly Ala Thr Gly Thr Ser Ala Ala Ala Arg Phe Gly  
 3540 3545 3550  
 40 Leu Glu Trp Lys Asp His Pro Phe Leu Ser Gly Ala Thr Pro Ile Ala  
 3555 3560 3565  
 Gly Ser Gly Ala Leu Leu Leu Thr Gly Arg Val Gly Leu Ala Ala His  
 3570 3575 3580  
 45 Pro Trp Leu Ala Asp His Ala Ile Ser Gly Thr Val Leu Leu Pro Gly  
 3585 3590 3595 3600  
 Thr Ala Ile Ala Asp Leu Leu Leu Arg Ala Val Glu Glu Val Gly Ala  
 3605 3610 3615  
 50 Gly Gly Val Glu Glu Leu Thr Leu His Glu Pro Leu Leu Leu Pro Glu  
 3620 3625 3630  
 Arg Gly Gly Leu His Val Gln Val Leu Val Glu Ala Ala Asp Glu Gln  
 3635 3640 3645  
 55

5 Gly Arg Arg Ala Val Ala Val Ala Ala Arg Pro Glu Gly Pro Gly Arg  
 3650 3655 3660  
 Asp Gly Glu Glu Gln Glu Trp Thr Arg His Ala Glu Gly Val Leu Thr  
 3665 3670 3675 3680  
 10 Ser Thr Glu Thr Ala Val Pro Asp Met Gly Trp Ala Ala Gly Ala Trp  
 3685 3690 3695  
 Pro Pro Pro Gly Ala Glu Pro Ile Asp Val Glu Glu Leu Tyr Asp Ala  
 3700 3705 3710  
 15 Phe Ala Ala Asp Gly Tyr Gly Tyr Gly Pro Ala Phe Thr Ala Leu Ser  
 3715 3720 3725  
 Gly Val Trp Arg Leu Gly Asp Glu Leu Phe Ala Glu Val Arg Arg Pro  
 3730 3735 3740  
 20 Ala Gly Gly Ala Gly Thr Thr Gly Asp Gly Phe Gly Val His Pro Ala  
 3745 3750 3755 3760  
 Leu Phe Asp Ala Ala Leu His Pro Trp Arg Ala Gly Gly Leu Leu Pro  
 3765 3770 3775  
 25 Asp Thr Gly Gly Thr Thr Trp Ala Pro Phe Ser Trp Gln Gly Ile Ala  
 3780 3785 3790  
 Leu His Thr Thr Gly Ala Glu Thr Leu Arg Val Arg Leu Ala Pro Ala  
 3795 3800 3805  
 30 Ala Gly Gly Thr Glu Ser Ala Phe Ser Val Gln Ala Ala Asp Pro Ala  
 3810 3815 3820  
 Gly Thr Pro Val Leu Thr Leu Asp Ala Leu Leu Leu Arg Pro Val Thr  
 3825 3830 3835 3840  
 35 Leu Gly Arg Ala Asp Ala Pro Gln Pro Leu Tyr Arg Val Asp Trp Gln  
 3845 3850 3855  
 Pro Val Gly Gln Gly Thr Glu Ala Ser Gly Ala Gln Gly Trp Thr Val  
 3860 3865 3870  
 40 Leu Gly Gln Ala Ala Ala Glu Thr Val Ala Gln Pro Ala Ala His Ala  
 3875 3880 3885  
 Asp Leu Thr Ala Leu Arg Thr Ala Val Ala Ala Ala Gly Thr Pro Val  
 3890 3895 3900  
 45 Pro Arg Leu Val Val Val Ser Pro Val Asp Thr Arg Leu Asp Glu Gly  
 3905 3910 3915 3920  
 50 Pro Val Leu Ala Asp Ala Glu Ala Arg Ala Arg Ala Gly Asp Gly Trp  
 3925 3930 3935  
 Asp Asp Asp Pro Leu Arg Val Ala Leu Gly Arg Gly Leu Thr Leu Val  
 3940 3945 3950  
 55 Arg Glu Trp Val Glu Asp Glu Arg Leu Ala Asp Ser Arg Leu Val Val  
 3955 3960 3965

5	Leu Thr Arg Gly Ala Val Ala Ala Gly Pro Gly Asp Val Pro Asp Leu 3970 3975 3980
	Thr Gly Ala Ala Leu Trp Gly Leu Leu Arg Ser Ala Gln Ser Glu Tyr 3985 3990 3995 4000
10	Pro Asp Arg Phe Thr Leu Ile Asp Val Asp Asp Ser Pro Glu Ser Arg 4005 4010 4015 Ala Ala Leu Pro Arg Ala Leu Gly Ser Ala Glu Arg Gln Leu Ala Leu 4020 4025 4030
15	Arg Thr Gly Asp Val Leu Ala Pro Ala Leu Val Pro Met Ala Thr Arg 4035 4040 4045
	Pro Ala Glu Thr Thr Pro Ala Thr Ala Val Ala Ser Ala Thr Thr Gln 4050 4055 4060
20	Thr Gln Val Thr Ala Pro Ala Pro Asp Asp Pro Ala Ala Asp Ala Val 4065 4070 4075 4080
	Phe Asp Pro Ala Gly Thr Val Leu Ile Thr Gly Gly Thr Gly Ala Leu 4085 4090 4095
25	Gly Arg Arg Val Ala Ser His Leu Ala Arg Arg Tyr Gly Val Arg His 4100 4105 4110
	Met Leu Leu Val Ser Arg Arg Gly Pro Asp Ala Pro Glu Ala Gly Pro 4115 4120 4125
30	Leu Glu Arg Glu Leu Ala Gly Leu Gly Val Thr Ala Thr Phe Leu Ala 4130 4135 4140
	Cys Asp Leu Thr Asp Ile Glu Ala Val Arg Lys Ala Val Ala Ala Val 4145 4150 4155 4160
35	Pro Ser Asp His Pro Leu Thr Gly Val Val His Thr Ala Gly Val Leu 4165 4170 4175
	Asp Asp Gly Ala Leu Thr Gly Leu Thr Arg Gln Arg Leu Asp Thr Val 4180 4185 4190
40	Leu Arg Pro Lys Ala Asp Ala Val Arg Asn Leu His Glu Ala Thr Leu 4195 4200 4205
	Asp Arg Pro Leu Arg Ala Phe Val Leu Phe Ser Ala Ala Ala Gly Leu 4210 4215 4220
45	Leu Gly Arg Pro Gly Gln Ala Ser Tyr Ala Ala Ala Asn Ala Val Leu 4225 4230 4235 4240
50	Asp Ala Leu Ala Gly Ala Arg Arg Ala Ala Gly Leu Pro Ala Val Ser 4245 4250 4255
	Leu Ala Trp Gly Leu Trp Asp Glu Gln Thr Gly Met Ala Gly Gly Leu 4260 4265 4270
55	Asp Glu Met Ala Leu Arg Val Leu Arg Arg Asp Gly Ile Ala Ala Met 4275 4280 4285

5 Pro Pro Glu Gln Gly Leu Glu Leu Leu Asp Leu Ala Leu Thr Gly His  
 4290 4295 4300  
 Arg Asp Gly Pro Ala Val Leu Val Pro Leu Leu Leu Asp Gly Ala Ala  
 4305 4310 4315 4320  
 10 Leu Arg Arg Thr Ala Lys Glu Arg Gly Ala Ala Thr Met Ser Pro Leu  
 4325 4330 4335  
 Leu Arg Ala Leu Leu Pro Ala Ala Leu Arg Arg Ser Gly Gly Ala Gly  
 4340 4345 4350  
 15 Ala Pro Ala Ala Ala Asp Arg His Gly Lys Glu Ala Asp Pro Gly Ala  
 4355 4360 4365  
 Gly Arg Leu Ala Gly Met Val Ala Leu Glu Ala Ala Glu Arg Ser Ala  
 4370 4375 4380  
 20 Ala Val Leu Glu Leu Val Thr Glu Gln Val Ala Glu Val Leu Gly Tyr  
 4385 4390 4395 4400  
 Ala Ser Ala Ala Glu Ile Glu Pro Glu Arg Pro Phe Arg Glu Ile Gly  
 4405 4410 4415  
 25 Val Asp Ser Leu Ala Ala Val Glu Leu Arg Asn Arg Leu Ser Arg Leu  
 4420 4425 4430  
 Val Gly Leu Arg Leu Pro Thr Thr Leu Ser Phe Asp His Pro Thr Pro  
 4435 4440 4445  
 30 Lys Asp Met Ala Gln His Ile Asp Gly Gln Leu Pro Arg Pro Ala Gly  
 4450 4455 4460  
 Ala Ser Pro Ala Asp Ala Ala Leu Glu Gly Ile Gly Asp Leu Ala Arg  
 4465 4470 4475 4480  
 35 Ala Val Ala Leu Leu Gly Thr Gly Asp Ala Arg Arg Ala Glu Val Arg  
 4485 4490 4495  
 Glu Gln Leu Val Gly Leu Leu Ala Ala Leu Asp Pro Pro Gly Arg Thr  
 4500 4505 4510  
 40 Gly Thr Ala Ala Pro Gly Val Pro Ser Gly Ala Asp Gly Ala Glu Pro  
 4515 4520 4525  
 45 Thr Val Thr Asp Arg Leu Asp Glu Ala Thr Asp Asp Glu Ile Phe Ala  
 4530 4535 4540  
 Phe Leu Asp Glu Gln Leu  
 4545 4550

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1996 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

5 Met Thr Ala Glu Asn Asp Lys Ile Arg Ser Tyr Leu Lys Arg Ala Thr  
 1 5 10 15  
 10 Ala Glu Leu His Arg Thr Lys Ser Arg Leu Ala Glu Val Glu Ser Ala  
 20 25 30  
 Ser Arg Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly  
 35 40 45  
 15 Gly Val Ala Ser Pro Asp Asp Leu Trp Asp Leu Val Ala Ala Gly Thr  
 50 55 60  
 Asp Ala Val Ser Ala Phe Pro Val Asp Arg Gly Trp Asp Val Glu Gly  
 65 70 75 80  
 20 Leu Tyr Asp Pro Asp Pro Glu Ala Val Gly Arg Ser Tyr Val Arg Glu  
 85 90 95  
 Gly Gly Phe Leu His Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe Gly  
 100 105 110  
 25 Ile Ser Pro Arg Glu Ala Ala Ala Met Asp Pro Gln Gln Arg Leu Leu  
 115 120 125  
 Leu Glu Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Val Pro Ala  
 130 135 140  
 30 Ser Leu Arg Gly Thr Arg Thr Gly Val Phe Thr Gly Val Met Tyr Asp  
 145 150 155 160  
 Asp Tyr Gly Ser Arg Phe Asp Ser Ala Pro Pro Glu Tyr Glu Gly Tyr  
 165 170 175  
 35 Leu Val Asn Gly Ser Ala Gly Ser Ile Ala Ser Gly Arg Val Ala Tyr  
 180 185 190  
 Ala Leu Gly Leu Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser  
 195 200 205  
 40 Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly  
 210 215 220  
 Glu Cys Asp Leu Ala Leu Ala Gly Gly Val Thr Val Met Ala Thr Pro  
 225 230 235 240  
 Thr Val Leu Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly  
 245 250 255  
 50 Arg Cys Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala Glu  
 260 265 270  
 Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn  
 275 280 285  
 55 Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp



	290	295	300
5	Gly Ala Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg 305 310 315 320		
	Val Ile Arg Glu Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp Val 325 330 335		
10	Asp Ala Val Glu Ala His Gly Thr Gly Thr Pro Leu Gly Asp Pro Ile 340 345 350		
	Glu Ala Gly Ala Leu Leu Ala Thr Tyr Gly Ser Glu Arg Gln Gly Gln 355 360 365		
15	Gly Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln 370 375 380		
	Ala Ala Ala Gly Val Gly Gly Val Ile Lys Val Val Gln Ala Met Arg 385 390 395 400		
20	His Gly Ser Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ser Lys 405 410 415		
	Val Glu Trp Ala Ser Gly Ala Val Glu Leu Leu Thr Glu Thr Arg Ser 420 425 430		
25	Trp Pro Arg Arg Val Glu Arg Val Arg Arg Ala Ala Val Ser Ala Phe 435 440 445		
	Gly Val Ser Gly Thr Asn Ala His Val Val Leu Glu Glu Ala Pro Ala 450 455 460		
30	Glu Ala Gly Ser Glu His Gly Asp Gly Pro Glu Pro Glu Arg Pro Asp 465 470 475 480		
	Ala Val Thr Gly Pro Leu Ser Trp Val Leu Ser Ala Arg Ser Glu Gly 485 490 495		
35	Ala Leu Arg Ala Gln Ala Val Arg Leu Arg Glu Cys Val Glu Arg Val 500 505 510		
	Gly Ala Asp Pro Arg Asp Val Ala Gly Ser Leu Val Val Ser Arg Ala 515 520 525		
	Ser Phe Gly Glu Arg Ala Val Val Val Gly Arg Gly Arg Glu Glu Leu 530 535 540		
40	Leu Ala Gly Leu Asp Val Val Ala Ala Gly Ala Pro Val Gly Val Ser 545 550 555 560		
	Gly Gly Val Ser Ser Gly Ala Gly Ala Val Val Arg Gly Ser Ala Val 565 570 575		
45	Arg Gly Arg Gly Val Gly Val Leu Phe Thr Gly Gln Gly Ala Gln Trp 580 585 590		
	Val Gly Met Gly Arg Gly Leu Tyr Ala Gly Gly Gly Val Phe Ala Glu 595 600 605		
50	Val Leu Asp Glu Val Leu Ser Val Val Gly Glu Val Gly Gly Trp Ser		

	610	615	620
5	Leu Arg Asp Val Met 625	Phe Gly Asp Val 630	Asp Val Asp Ala Gly Ala Gly 635 640
	Ala Asp Ala Gly Val 645	Gly Ser Gly Val 650	Gly Gly Leu Leu Gly 655
10	Arg Thr Glu Phe Ala Gln Pro 660	Ala Leu Phe Ala Leu Glu 665	Val Ala Leu 670
	Phe Arg Ala Leu Glu Ala Arg 675	Gly Val Glu Val Ser 680	Val Val Leu Gly 685
15	His Ser Val Gly Glu Val 690	Ala Ala Ala Tyr 695	Val Ala Gly Val Leu Ser 700
	Leu Gly Asp Ala Val Arg 705	Leu Val Val Ala 710	Arg Gly Gly Leu Met Gly 715 720
20	Gly Leu Pro Val Gly Gly Gly Met Trp 725	Ser Val Gly Ala Ser Glu Ser 730	
	Val Val Arg Gly Val Val Glu Gly 740	Leu Gly Glu Trp Val Ser Val Ala 745	
25	Ala Val Asn Gly Pro Arg Ser Val Val Leu Ser Gly Asp Val Gly Val 755		765
	Leu Glu Ser Val Val Ala Ser Leu Met Gly Asp Gly Val Glu Cys Arg 770	775	780
30	Arg Leu Asp Val Ser His Gly Phe His Ser Val Leu Met Glu Pro Val 785	790	795 800
	Leu Gly Glu Phe Arg Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val 805	810	815
35	Arg Pro Gly Val Val Val Val Ser Ser Val Ser Gly Gly Val Val Gly 820	825	830
	Ser Gly Glu Leu Gly Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu 835	840	845
40	Ala Val Arg Phe Ala Asp Gly Val Gly Val Val Arg Gly Leu Gly Val 850	855	860
	Gly Thr Leu Val Glu Val Gly Pro His Gly Val Leu Thr Gly Met Ala 865	870	875 880
45	Gly Glu Cys Leu Gly Ala Gly Asp Asp Val Val Val Val Pro Ala Met 885	890	895
50	Arg Arg Gly Arg Ala Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr 900	905	910
	Val Phe Thr Arg Asp Ala Gly Leu Asp Ala Thr Thr Leu His Thr Gly 915	920	925
55	Ser Thr Gly Arg Arg Ile Asp Leu Pro Thr Tyr Pro Phe Gln His Asp		

	930	935	940
5	Arg Tyr Trp Leu Ala Ala Pro Ser Arg Pro Arg Thr Asp Gly Leu Ser 945 950 955 960		
	Ala Ala Gly Leu Arg Glu Val Glu His Pro Leu Leu Thr Ala Ala Val 965 970 975		
10	Glu Leu Pro Gly Thr Asp Thr Glu Val Trp Thr Gly Arg Ile Ser Ala 980 985 990		
	Ala Asp Leu Pro Trp Leu Ala Asp His Leu Val Trp Asp Arg Gly Val 995 1000 1005		
15	Val <sup>*</sup> Pro Gly Thr Ala Leu Leu Glu Thr Val Leu Gln Val Gly Ser Arg 1010 1015 1020		
	Ile Gly Leu Pro Arg Val Ala Glu Leu Val Leu Glu Thr Pro Leu Thr 1025 1030 1035 1040		
20	Trp Thr Ser Asp Arg Pro Leu Gln Val Arg Ile Val Val Thr Ala Ala 1045 1050 1055		
	Ala Thr Ala Pro Gly Gly Ala Arg Glu Leu Thr Leu His Ser Arg Pro 1060 1065 1070		
25	Glu Pro Val Ala Ala Ser Ser Ser Ser Pro Ser Pro Ala Ser Pro Arg 1075 1080 1085		
	His Leu Thr Ala Gln Glu Ser Asp Asp Asp Trp Thr Arg His Ala Ser 1090 1095 1100		
30	Gly Leu Leu Ala Pro Ala Ala Gly Leu Ala Asp Asp Phe Ala Glu Leu 1105 1110 1115 1120		
	Thr Gly Ala Trp Pro Pro Val Gly Ala Glu Pro Leu Asp Leu Ala Gly 1125 1130 1135		
35	Gln Tyr Pro Leu Phe Ala Ala Ala Gly Val Arg Tyr Glu Gly Ala Phe 1140 1145 1150		
	Arg Gly Leu Arg Ala Ala Trp Arg Arg Gly Asp Glu Val Phe Ala Asp 1155 1160 1165		
40	Val Arg Leu Pro Asp Ala His Ala Val Asp Ala Asp Arg Tyr Gly Val 1170 1175 1180		
	His Pro Ala Leu Leu Asp Ala Val Leu His Pro Ile Ala Ser Leu Asp 1185 1190 1195 1200		
45	Pro Leu Gly Asp Gly Gly His Gly Leu Leu Pro Phe Ser Trp Thr Asp 1205 1210 1215		
50	Val Gln Gly His Gly Ala Gly Gly His Ala Leu Arg Val Arg Val Ala 1220 1225 1230		
	Ala Val Asp Gly Gly Ala Val Ser Val Thr Ala Ala Asp His Ala Gly 1235 1240 1245		
55	Asn Pro Val Leu Ser Ala Arg Ser Leu Ala Leu Arg Arg Ile Thr Ala		

	1250	1255	1260
5	Asp Arg Leu Pro Ala Ala Pro Val Ala Pro Leu Tyr Arg Val Asp Trp 1265	1270	1275 1280
	Leu Pro Phe Pro Gly Pro Val Pro Val Ser Ala Gly Gly Arg Trp Ala 1285	1290	1295
10	Val Val Gly Pro Glu Ala Glu Ala Thr Ala Ala Gly Leu Arg Ala Val 1300	1305	1310
	Gly Leu Asp Val Arg Thr His Ala Leu Pro Leu Gly Glu Pro Leu Pro 1315	1320	1325
15	Pro Gln Ala Gly Thr Asp Ala Glu Val Ile Ile Leu Asp Leu Thr Thr 1330	1335	1340
	Thr Ala Ala Gly Arg Thr Ala Ser Asp Gly Gly Arg Leu Ser Leu Leu 1345	1350	1355 1360
20	Asp Glu Val Arg Ala Thr Val Arg Arg Thr Leu Glu Ala Val Gln Ala 1365	1370	1375
	Arg Leu Ala Asp Thr Glu Thr Ala Pro Asp Val Asp Val Arg Thr Ala 1380	1385	1390
25	Ala Arg Pro Arg Thr Ala Ala Arg Thr Ser Pro Arg Val Asp Thr Arg 1395	1400	1405
	Thr Gly Ala Arg Thr Ala Asp Gly Pro Arg Leu Val Val Leu Thr Arg 1410	1415	1420
	Gly Ala Ala Gly Pro Glu Gly Gly Ala Ala Asp Pro Ala Gly Ala Ala 1425	1430	1435 1440
35	Val Trp Gly Leu Val Arg Val Ala Gln Ala Glu Gln Pro Gly Arg Phe 1445	1450	1455
	Thr Leu Val Asp Val Asp Gly Thr Gln Ala Ser Leu Arg Ala Leu Pro 1460	1465	1470
40	Gly Leu Leu Ala Thr Asp Ala Gly Gln Ser Ala Val Arg Asp Gly Arg 1475	1480	1485
	Val Thr Val Pro Arg Leu Val Pro Val Ala Asp Pro Val Pro His Gly 1490	1495	1500
45	Gly Gly Thr Ala Ala Asp Gly Thr Gly Ala Gly Glu Pro Ser Ala Thr 1505	1510	1515 1520
	Leu Asp Pro Glu Gly Thr Val Leu Ile Thr Gly Gly Thr Gly Ala Leu 1525	1530	1535
50	Ala Ala Glu Thr Ala Arg His Leu Val Asp Arg His Lys Val Arg His 1540	1545	1550
	Leu Leu Leu Val Gly Arg Arg Gly Pro Asp Ala Pro Gly Val Asp Arg 1555	1560	1565
55	Leu Val Ala Glu Leu Thr Glu Ser Gly Ala Glu Val Ala Val Arg Ala		

	1570	1575	1580
5	Cys Asp Val Thr Asp Arg Asp Ala Leu Arg Arg Leu Leu Asp Ala Leu 1585 1590 1595 1600		
	Pro Asp Glu His Pro Leu Thr Cys Val Val His Thr Ala Gly Val Leu 1605 1610 1615		
10	Asp Asp Gly Val Leu Ser Ala Gln Thr Ala Glu Arg Ile Asp Thr Val 1620 1625 1630		
	Leu Arg Pro Lys Ala Asp Ala Ala Val His Leu Asp Glu Leu Thr Arg 1635 1640 1645		
15	Glu Ile Gly Arg Val Pro Leu Val Leu Tyr Ser Ser Val Ser Ala Thr 1650 1655 1660		
	Leu Gly Ser Ala Gly Gln Ala Gly Tyr Ala Ala Ala Asn Ala Phe Met 1665 1670 1675 1680		
20	Asp Ala Leu Ala Ala Arg Arg Cys Ala Ala Gly His Pro Ala Leu Ser 1685 1690 1695		
25	Leu Gly Trp Gly Trp Trp Ser Gly Val Gly Leu Ala Thr Gly Leu Asp 1700 1705 1710		
	Gly Ala Asp Ala Ala Arg Val Arg Arg Ser Gly Leu Ala Pro Leu Asp 1715 1720 1725		
30	Ala Gly Ala Ala Leu Asp Leu Leu Asp Arg Ala Leu Thr Arg Pro Glu 1730 1735 1740		
	Pro Ala Leu Leu Pro Val Arg Leu Asp Leu Arg Ala Ala Ala Gly Ala 1745 1750 1755 1760		
35	Thr Ala Leu Pro Glu Val Leu Arg Asp Leu Ala Gly Val Pro Ala Asp 1765 1770 1775		
	Ala Arg Ser Thr Pro Gly Ala Ala Ala Gly Thr Gly Asp Glu Asp Gly 1780 1785 1790		
40	Ala Val Arg Pro Ala Pro Ala Pro Ala Asp Ala Ala Gly Thr Leu Ala 1795 1800 1805		
	Ala Arg Leu Ala Gly Arg Ser Ala Pro Glu Arg Thr Ala Leu Leu Leu 1810 1815 1820		
45	Asp Leu Val Arg Thr Glu Val Ala Ala Val Leu Gly His Gly Asp Pro 1825 1830 1835 1840		
	Ala Ala Ile Gly Ala Ala Arg Thr Phe Lys Asp Ala Gly Phe Asp Ser 1845 1850 1855		
50	Leu Thr Ala Val Asp Leu Arg Asn Arg Leu Asn Thr Arg Thr Gly Leu 1860 1865 1870		
	Arg Leu Pro Ala Thr Leu Val Phe Asp His Pro Thr Pro Leu Ala Leu 1875 1880 1885		
55	Ala Glu Leu Leu Leu Asp Gly Leu Glu Ala Ala Gly Pro Ala Glu Pro		

	1890	1895	1900
5	Ala Ala Glu Val Pro Asp Glu Ala Ala Gly Ala Glu Thr Leu Ser Gly 1905	1910	1915 1920
	Val Ile Asp Arg Leu Glu Arg Ser Leu Ala Ala Thr Asp Asp Gly Asp 1925	1930	1935
10	Ala Arg Val Arg Ala Ala Arg Arg Leu Arg Gly Leu Leu Asp Ala Leu 1940	1945	1950
	Pro Ala Gly Pro Gly Ala Ala Ser Gly Pro Asp Ala Gly Glu His Ala 1955	1960	1965
15	Pro Gly Arg Gly Asp Val Val Ile Asp Arg Leu Arg Ser Ala Ser Asp 1970	1975	1980
	Asp Asp Leu Phe Asp Leu Leu Asp Ser Asp Phe Gln 1985	1990	1995
20			

## (2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3724 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Ser Ala Thr Asn Glu Glu Lys Leu Arg Glu Tyr Leu Arg Arg Ala 1	5	10	15
Met Ala Asp Leu His Ser Ala Arg Glu Arg Leu Arg Glu Val Glu Ser 20	25	30	
Ala Ser Arg Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro 35	40	45	
Gly Gly Val Ala Ser Pro Glu Glu Leu Trp Asp Leu Val Ala Ala Gly 50	55	60	
Thr Asp Ala Ile Ser Pro Phe Pro Val Asp Arg Gly Trp Asp Ala Glu 65	70	75	80
Gly Leu Tyr Asp Pro Glu Pro Gly Val Pro Gly Lys Ser Tyr Val Arg 85	90	95	
Glu Gly Gly Phe Leu His Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe 100	105	110	
Gly Ile Ser Pro Arg Glu Ala Ala Ala Met Asp Pro Gln Gln Arg Leu 115	120	125	
Leu Leu Glu Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Val Pro 130	135	140	

Ala Ser Leu Arg Gly Thr Arg Thr Gly Val Phe Thr Gly Val Met Tyr  
 145 150 155 160  
 5 His Asp Tyr Gly Ser His Gln Val Gly Thr Ala Ala Asp Pro Ser Gly  
 165 170 175  
 Gln Leu Gly Leu Gly Thr Ala Gly Ser Val Ala Ser Gly Arg Val Ala  
 180 185 190  
 10 Tyr Thr Leu Gly Leu Gln Gly Pro Ala Val Thr Met Asp Thr Ala Cys  
 195 200 205  
 Ser Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg  
 210 215 220  
 Gly Glu Cys Asp Leu Ala Leu Ala Gly Gly Ala Thr Val Leu Ala Thr  
 225 230 235 240  
 20 Pro Thr Val Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp  
 245 250 255  
 Gly Arg Cys Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala  
 260 265 270  
 25 Glu Gly Ala Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg  
 275 280 285  
 Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln  
 290 295 300  
 30 Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln  
 305 310 315 320  
 Arg Val Ile Arg Asp Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp  
 325 330 335  
 35 Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Pro Leu Gly Asp Pro  
 340 345 350  
 Ile Glu Ala Gly Ala Leu Met Ala Thr Tyr Gly Ser Glu Arg Val Gly  
 355 360 365  
 40 Asp Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr Gln  
 370 375 380  
 Ala Ala Ala Gly Ala Ala Gly Val Ile Lys Met Val Gln Ala Leu Arg  
 385 390 395 400  
 45 Gln Ser Glu Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ala Lys  
 405 410 415  
 Val Glu Trp Asp Ala Gly Ala Val Gln Leu Leu Thr Gly Val Arg Pro  
 420 425 430  
 50 Trp Pro Arg Arg Glu His Arg Pro Arg Arg Ala Ala Val Ser Ala Phe  
 435 440 445  
 55 Gly Val Ser Gly Thr Asn Ala His Val Ile Ile Glu Glu Pro Pro Ala  
 450 455 460

Ala Gly Asp Thr Ser Pro Ala Gly Asp Thr Pro Glu Pro Gly Glu Ala  
 465 470 475 480  
 5 Thr Ala Ser Pro Ser Thr Ala Ala Gly Pro Ser Ser Pro Ser Ala Val  
 485 490 495  
 Ala Gly Pro Leu Ser Pro Ser Ser Pro Ala Val Val Trp Pro Leu Ser  
 500 505 510  
 10 Ala Glu Thr Ala Pro Ala Leu Arg Ala Gln Ala Ala Arg Leu Arg Ala  
 515 520 525  
 His Leu Glu Arg Leu Pro Gly Thr Ser Pro Thr Asp Ile Gly His Ala  
 530 535 540  
 15 Leu Ala Ala Glu Arg Ala Ala Leu Thr Arg Arg Val Val Leu Leu Gly  
 545 550 555 560  
 Asp Asp Gly Ala Pro Val Asp Ala Leu Ala Ala Leu Ala Ala Gly Glu  
 565 570 575  
 20 Thr Thr Pro Asp Ala Val His Gly Thr Ala Ala Asp Ile Arg Arg Val  
 580 585 590  
 Ala Phe Val Phe Pro Gly Gln Gly Ser Gln Trp Ala Gly Met Gly Ala  
 595 600 605  
 Glu Leu Leu Asp Thr Ala Pro Ala Phe Ala Ala Glu Leu Asp Arg Cys  
 610 615 620  
 30 Gln Gly Ala Leu Ser Pro Tyr Val Asp Trp Asn Leu Ala Asp Val Leu  
 625 630 635 640  
 Arg Gly Ala Pro Ala Ala Pro Gly Leu Asp Arg Val Asp Val Val Gln  
 645 650 655  
 35 Pro Ala Thr Phe Ala Val Met Val Gly Leu Ala Ala Leu Trp Arg Ser  
 660 665 670  
 Leu Gly Val Glu Pro Ala Ala Val Ile Gly His Ser Gln Gly Glu Ile  
 675 680 685  
 40 Ala Ala Ala Cys Val Ala Gly Ala Leu Ser Leu Glu Asp Ala Ala Arg  
 690 695 700  
 Ile Val Ala Leu Arg Ser Gln Val Ile Ala Arg Glu Leu Ala Gly Arg  
 705 710 715 720  
 45 Gly Gly Met Ala Ser Val Ala Leu Pro Ala Ala Glu Val Glu Ala Arg  
 725 730 735  
 Leu Ala Gly Gly Val Glu Ile Ala Ala Val Asn Gly Pro Gly Ser Thr  
 740 745 750  
 50 Val Val Cys Gly Glu Pro Gly Ala Leu Glu Ala Leu Leu Val Thr Leu  
 755 760 765  
 55 Glu Ser Glu Gly Thr Arg Val Arg Arg Ile Asp Val Asp Tyr Ala Ser  
 770 775 780



5	His Ser His Tyr Val Glu Ser Ile Arg Ala Glu Leu Ala Thr Val Leu 785 790 795 800
	Gly Pro Val Arg Pro Arg Arg Gly Asp Val Pro Phe Tyr Ser Thr Val 805 810 815
10	Glu Ala Ala Leu Leu Asp Thr Ala Thr Leu Asp Ala Asp Tyr Trp Tyr 820 825 830
	Arg Asn Leu Arg Leu Pro Val Arg Phe Glu Pro Thr Val Arg Ala Met 835 840 845
15	Leu Asp Asp Gly Val Asp Ala Phe Val Glu Cys Ser Ala His Pro Val 850 855 860
	Leu Thr Val Gly Val Arg Gln Thr Val Glu Ser Ala Gly Gly Ala Val 865 870 875 880
20	Pro Ala Leu Ala Ser Leu Arg Arg Asp Glu Gly Gly Leu Arg Arg Phe 885 890 895
	Leu Thr Ser Ala Ala Glu Ala Gln Val Val Gly Val Pro Val Asp Trp 900 905 910
25	Ala Thr Leu Arg Pro Gly Ala Gly Arg Val Asp Leu Pro Thr Tyr Ala 915 920 925
	Phe Gln Arg Glu Arg His Trp Val Gly Pro Ala Arg Pro Asp Ser Ala 930 935 940
30	Ala Thr Ala Ala Thr Thr Gly Asp Asp Ala Pro Glu Pro Gly Asp Arg 945 950 955 960
	Leu Gly Tyr His Val Ala Trp Lys Gly Leu Arg Ser Thr Thr Gly Gly 965 970 975
35	Trp Arg Pro Gly Leu Arg Leu Leu Ile Val Pro Thr Gly Asp Gln Tyr 980 985 990
	Thr Ala Leu Ala Asp Thr Leu Glu Gln Ala Val Ala Ser Phe Gly Gly 995 1000 1005
40	Thr Val Arg Arg Val Ala Phe Asp Pro Ala Arg Thr Gly Arg Ala Glu 1010 1015 1020
	Leu Phe Gly Leu Leu Glu Thr Glu Ile Asn Gly Asp Thr Ala Val Thr 1025 1030 1035 1040
45	Gly Val Val Ser Leu Leu Gly Leu Cys Thr Asp Gly Arg Pro Asp His 1045 1050 1055
	Pro Ala Val Pro Val Ala Val Thr Ala Thr Leu Ala Leu Val Gln Ala 1060 1065 1070
50	Leu Ala Asp Leu Gly Ser Thr Ala Pro Leu Trp Thr Val Thr Cys Gly 1075 1080 1085
55	Ala Val Ala Thr Ala Pro Asp Glu Leu Pro Cys Thr Ala Gly Ala Gln 1090 1095 1100

5 Leu Trp Gly Leu Gly Arg Val Ala Ala Leu Glu Leu Pro Glu Val Trp  
 1105 1110 1115 1120  
 Gly Gly Leu Ile Asp Leu Pro Ala Arg Pro Asp Ala Arg Val Leu Asp  
 1125 1130 1135  
 10 Arg Leu Ala Gly Val Leu Ala Glu Pro Gly Gly Glu Asp Gln Ile Ala  
 1140 1145 1150  
 Val Arg Met Ala Gly Val Phe Gly Arg Arg Val Leu Arg Asn Pro Ala  
 1155 1160 1165  
 15 Asp Ser Arg Pro Pro Ala Trp Arg Ala Arg Gly Thr Val Leu Ile Ala  
 1170 1175 1180  
 Gly Asp Leu Thr Thr Val Pro Gly Arg Leu Val Arg Ser Leu Leu Glu  
 1185 1190 1195 1200  
 20 Asp Gly Ala Asp Arg Val Val Leu Ala Gly Pro Asp Ala Pro Ala Gln  
 1205 1210 1215  
 Ala Ala Ala Ala Gly Leu Thr Gly Val Ser Leu Val Pro Val Arg Cys  
 1220 1225 1230  
 25 Asp Val Thr Asp Arg Ala Ala Leu Ala Ala Leu Leu Asp Glu His Ala  
 1235 1240 1245  
 Pro Thr Val Ala Val His Ala Pro Pro Leu Val Pro Leu Ala Pro Leu  
 1250 1255 1260  
 30 Arg Glu Thr Ala Pro Gly Asp Ile Ala Ala Ala Leu Ala Ala Lys Thr  
 1265 1270 1275 1280  
 Thr Ala Ala Gly His Leu Val Asp Leu Ala Pro Ala Ala Gly Leu Asp  
 1285 1290 1295  
 35 Ala Leu Val Leu Phe Ser Ser Val Ser Gly Val Trp Gly Gly Ala Ala  
 1300 1305 1310  
 Gln Gly Gly Tyr Ala Ala Ala Ser Ala His Leu Asp Ala Leu Ala Glu  
 1315 1320 1325  
 40 Arg Ala Arg Ala Ala Gly Val Pro Ala Phe Ser Val Ala Trp Ser Pro  
 1330 1335 1340  
 Trp Ala Gly Gly Thr Pro Ala Asp Gly Ala Glu Ala Glu Phe Leu Ser  
 1345 1350 1355 1360  
 Arg Arg Gly Leu Ala Pro Leu Asp Pro Asp Gln Ala Val Arg Thr Leu  
 1365 1370 1375  
 50 Arg Arg Met Leu Glu Arg Gly Ser Ala Cys Gly Ala Val Ala Asp Val  
 1380 1385 1390  
 Glu Trp Ser Arg Phe Ala Ala Ser Tyr Thr Trp Val Arg Pro Ala Val  
 1395 1400 1405  
 55 Leu Phe Asp Asp Ile Pro Asp Val Gln Arg Leu Arg Ala Ala Glu Leu  
 1410 1415 1420

Ala Pro Ser Thr Gly Asp Ser Thr Thr Ser Glu Leu Val Arg Glu Leu  
 1425 1430 1435 1440  
 5 Thr Ala Gln Ser Gly His Lys Arg His Ala Thr Leu Leu Arg Leu Val  
 1445 1450 1455  
 Arg Ala His Ala Ala Ala Val Leu Gly Gln Ser Ser Gly Asp Ala Val  
 1460 1465 1470  
 10 Ser Ser Ala Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala  
 1475 1480 1485  
 Leu Glu Leu Arg Asp Arg Leu Ser Thr Ser Thr Gly Leu Lys Leu Pro  
 1490 1495 1500  
 15 Thr Ser Leu Val Phe Asp His Ser Ser Pro Ala Ala Leu Ala Arg His  
 1505 1510 1515 1520  
 Leu Gly Glu Glu Leu Leu Gly Arg Asn Asp Thr Ala Asp Arg Ala Gly  
 1525 1530 1535  
 20 Pro Asp Thr Pro Val Arg Thr Asp Glu Pro Ile Ala Ile Ile Gly Met  
 1540 1545 1550  
 Ala Cys Arg Leu Pro Gly Gly Val Gln Ser Pro Glu Asp Leu Trp Asp  
 1555 1560 1565  
 25 Leu Leu Thr Gly Gly Thr Asp Ala Ile Thr Pro Phe Pro Thr Asn Arg  
 1570 1575 1580  
 Gly Trp Asp Asn Glu Thr Leu Tyr Asp Pro Asp Pro Asp Ser Pro Gly  
 1585 1590 1595 1600  
 30 His His Thr Tyr Val Arg Glu Gly Gly Phe Leu His Asp Ala Ala Glu  
 1605 1610 1615  
 Phe Asp Pro Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met  
 1620 1625 1630  
 Asp Pro Gln Gln Arg Leu Ile Leu Glu Thr Ser Trp Glu Ser Phe Glu  
 1635 1640 1645  
 40 Arg Ala Gly Ile Asp Pro Val Glu Leu Arg Gly Ser Arg Thr Gly Val  
 1650 1655 1660  
 Phe Val Gly Thr Asn Gly Gln His Tyr Val Pro Leu Leu Gln Asp Gly  
 1665 1670 1675 1680  
 45 Asp Glu Asn Phe Asp Gly Tyr Ile Ala Thr Gly Asn Ser Ala Ser Val  
 1685 1690 1695  
 Met Ser Gly Arg Leu Ser Tyr Val Phe Gly Leu Glu Gly Pro Ala Val  
 1700 1705 1710  
 50 Thr Val Asp Thr Ala Cys Ser Ala Ser Leu Ala Ala Leu His Leu Ala  
 1715 1720 1725  
 Val Gln Ser Leu Arg Arg Gly Glu Cys Asp Tyr Ala Leu Ala Gly Gly  
 1730 1735 1740

Ala Thr Val Met Ser Thr Pro Glu Met Leu Val Glu Phe Ala Arg Gln  
 1745 1750 1755 1760

5 Arg Ala Val Ser Pro Asp Gly Arg Ser Lys Ala Phe Ala Glu Ala Ala  
 1765 1770 1775

Asp Gly Val Gly Leu Ala Glu Gly Ala Gly Met Leu Leu Val Glu Arg  
 1780 1785 1790

10 Leu Ser Glu Ala Gln Lys Lys Gly His Pro Val Leu Ala Val Val Arg  
 1795 1800 1805

Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro  
 1810 1815 1820

15 Ser Gly Pro Ala Gln Gln Arg Val Ile Arg Glu Ala Leu Ala Asp Ala  
 1825 1830 1835 1840

Gly Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly  
 20 1845 1850 1855

Thr Pro Leu Gly Asp Pro Ile Glu Ala Gly Ala Leu Leu Ala Thr Tyr  
 1860 1865 1870

25 Gly Arg Asp Arg Arg Asp Gly Pro Leu Trp Leu Gly Ser Leu Lys Ser  
 1875 1880 1885

Asn Ile Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys  
 1890 1895 1900

30 Met Val Leu Ala Leu Arg His Gly Glu Leu Pro Arg Thr Leu His Ala  
 1905 1910 1915 1920

Ser Thr Ala Ser Ser Arg Ile Asp Trp Asp Ala Gly Ala Val Glu Leu  
 1925 1930 1935

35 Leu Asp Glu Ala Arg Pro Trp Leu Gln Arg Ala Glu Gly Pro Arg Arg  
 1940 1945 1950

Ala Gly Ile Ser Ser Phe Gly Ile Ser Gly Thr Asn Ala His Leu Val  
 1955 1960 1965

40 Ile Glu Glu Pro Pro Glu Pro Thr Ala Pro Glu Leu Leu Ala Pro Glu  
 1970 1975 1980

Pro Ala Ala Asp Gly Asp Val Trp Ser Glu Glu Trp Trp His Glu Val  
 45 1985 1990 1995 2000

Thr Val Pro Leu Met Met Ser Ala His Asn Glu Ala Ala Leu Arg Asp  
 2005 2010 2015

50 Gln Ala Arg Arg Leu Arg Ala Asp Leu Leu Ala His Pro Glu Leu His  
 2020 2025 2030

Pro Ala Asp Val Gly Tyr Thr Leu Ile Thr Thr Arg Thr Arg Phe Glu  
 2035 2040 2045

55 Gln Arg Ala Ala Val Val Gly Glu Asn Phe Thr Glu Leu Ile Ala Ala  
 2050 2055 2060

Leu Asp Asp Leu Val Glu Gly Arg Pro His Pro Leu Val Leu Arg Gly  
 2065 2070 2075 2080  
 5 Thr Ala Gly Thr Ser Asp Gln Val Val Phe Val Phe Pro Gly Gln Gly  
 2085 2090 2095  
 Ser Gln Trp Pro Glu Met Ala Asp Gly Leu Leu Ala Arg Ser Ser Gly  
 2100 2105 2110  
 10 Ser Gly Ser Phe Leu Glu Thr Ala Arg Ala Cys Asp Leu Ala Leu Arg  
 2115 2120 2125  
 Pro His Leu Gly Trp Ser Val Leu Asp Val Leu Arg Arg Glu Pro Gly  
 2130 2135 2140  
 15 Ala Pro Ser Leu Asp Arg Val Asp Val Val Gln Pro Val Leu Phe Thr  
 2145 2150 2155 2160  
 Met Met Val Ser Leu Ala Glu Thr Trp Arg Ser Leu Gly Val Glu Pro  
 2165 2170 2175  
 20 Ala Ala Val Val Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val  
 2180 2185 2190  
 25 Ala Gly Ala Leu Thr Leu Asp Asp Ala Ala Arg Ile Val Ala Leu Arg  
 2195 2200 2205  
 Ser Gln Ala Trp Leu Arg Leu Ala Gly Lys Gly Gly Met Val Ala Val  
 2210 2215 2220  
 30 Thr Leu Ser Glu Arg Asp Leu Arg Pro Arg Leu Glu Pro Trp Ser Asp  
 2225 2230 2235 2240  
 Arg Leu Ala Val Ala Ala Val Asn Gly Pro Glu Thr Cys Ala Val Ser  
 2245 2250 2255  
 35 Gly Asp Pro Asp Ala Leu Ala Glu Leu Val Ala Glu Leu Gly Ala Glu  
 2260 2265 2270  
 Gly Val His Ala Arg Pro Ile Pro Gly Val Asp Thr Ala Gly His Ser  
 2275 2280 2285  
 40 Pro Gln Val Asp Thr Leu Glu Ala His Leu Arg Lys Val Leu Ala Pro  
 2290 2295 2300  
 Val Ala Pro Arg Thr Ser Asp Ile Pro Phe Tyr Ser Thr Val Thr Gly  
 2305 2310 2315 2320  
 45 Gly Leu Ile Asp Thr Ala Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn  
 2325 2330 2335  
 Met Arg Glu Pro Val Glu Phe Glu Gln Ala Thr Arg Ala Leu Ile Ala  
 2340 2345 2350  
 50 Asp Gly His Asp Val Phe Leu Glu Ser Ser Pro His Pro Met Leu Ala  
 2355 2360 2365  
 55 Val Ser Leu Gln Glu Thr Ile Ser Asp Ala Gly Ser Pro Ala Ala Val  
 2370 2375 2380

Leu Gly Thr Leu Arg Arg Gly Gln Gly Gly Pro Arg Trp Leu Gly Val  
 2385 2390 2395 2400  
 5 Ala Leu Cys Arg Ala Tyr Thr His Gly Leu Glu Ile Asp Ala Glu Ala  
 2405 2410 2415  
 Ile Phe Gly Pro Asp Ser Arg Gln Val Glu Leu Pro Thr Tyr Pro Phe  
 2420 2425 2430  
 10 Gln Arg Glu Arg Tyr Trp Tyr Ser Pro Gly His Arg Gly Asp Asp Pro  
 2435 2440 2445  
 Ala Ser Leu Gly Leu Asp Ala Val Asp His Pro Leu Leu Gly Ser Gly  
 2450 2455 2460  
 15 Val Glu Leu Pro Glu Ser Gly Asp Arg Met Tyr Thr Ala Arg Leu Gly  
 2465 2470 2475 2480  
 Ala Asp Thr Thr Pro Trp Leu Ala Asp His Ala Leu Leu Gly Ser Pro  
 2485 2490 2495  
 20 Leu Leu Pro Gly Ala Ala Phe Ala Asp Leu Ala Leu Trp Ala Gly Arg  
 2500 2505 2510  
 25 Gln Ala Gly Thr Gly Arg Val Glu Glu Leu Thr Leu Ala Ala Pro Leu  
 2515 2520 2525  
 Val Leu Pro Gly Ser Gly Gly Val Arg Leu Arg Leu Asn Val Gly Ala  
 2530 2535 2540  
 30 Pro Gly Thr Asp Asp Ala Arg Arg Phe Ala Val His Ala Arg Ala Glu  
 2545 2550 2555 2560  
 Gly Ala Thr Asp Trp Thr Leu His Ala Glu Gly Leu Leu Thr Ala Gln  
 2565 2570 2575  
 35 Asp Thr Ala Asp Ala Pro Asp Ala Ser Ala Ala Thr Pro Pro Pro Gly  
 2580 2585 2590  
 Ala Glu Gln Leu Asp Ile Gly Asp Phe Tyr Gln Arg Phe Ser Glu Leu  
 2595 2600 2605  
 40 Gly Tyr Gly Tyr Gly Pro Phe Phe Arg Gly Leu Val Ser Ala His Arg  
 2610 2615 2620  
 Cys Gly Pro Asp Ile His Ala Glu Val Ala Leu Pro Val Gln Ala Gln  
 2625 2630 2635 2640  
 45 Gly Asp Ala Ala Arg Phe Gly Ile His Pro Ala Leu Leu Asp Ala Ala  
 2645 2650 2655  
 Leu Gln Thr Met Ser Leu Gly Gly Phe Phe Pro Glu Asp Gly Arg Val  
 2660 2665 2670  
 50 Arg Met Pro Phe Ala Leu Arg Gly Val Arg Leu Tyr Arg Ala Gly Ala  
 2675 2680 2685  
 55 Asp Arg Leu His Val Arg Val Ser Pro Val Ser Glu Asp Ala Val Arg  
 2690 2695 2700

Ile Arg Cys Ala Asp Gly Glu Gly Arg Pro Val Ala Glu Ile Glu Ser  
 2705 2710 2715 2720  
 5 Phe Ile Met Arg Pro Val Asp Pro Gly Gln Leu Leu Gly Gly Arg Pro  
 2725 2730 2735  
 Val Gly Ala Asp Ala Leu Phe Arg Ile Ala Trp Arg Glu Leu Ala Ala  
 2740 2745 2750  
 10 Gly Pro Gly Thr Arg Thr Gly Asp Gly Thr Pro Pro Pro Val Arg Trp  
 2755 2760 2765  
 Val Leu Ala Gly Pro Asp Ala Leu Gly Leu Ala Glu Ala Ala Asp Ala  
 2770 2775 2780  
 15 His Leu Pro Ala Val Pro Gly Pro Asp Gly Ala Leu Pro Ser Pro Thr  
 2785 2790 2795 2800  
 Gly Arg Pro Ala Pro Asp Ala Val Val Phe Ala Val Arg Ala Gly Thr  
 2805 2810 2815  
 20 Gly Asp Val Ala Ala Asp Ala His Thr Val Ala Cys Arg Val Leu Asp  
 2820 2825 2830  
 Leu Val Gln Arg Arg Leu Ala Ala Pro Glu Gly Pro Asp Gly Ala Arg  
 2835 2840 2845  
 Leu Val Val Ala Thr Arg Gly Ala Val Ala Val Arg Asp Asp Ala Glu  
 2850 2855 2860  
 30 Val Asp Asp Pro Ala Ala Ala Ala Trp Gly Leu Leu Arg Ser Ala  
 2865 2870 2875 2880  
 Gln Ala Glu Glu Pro Gly Arg Phe Leu Leu Val Asp Leu Asp Asp Asp  
 2885 2890 2895  
 35 Pro Ala Ser Ala Arg Ala Leu Thr Asp Ala Leu Ala Ser Gly Glu Pro  
 2900 2905 2910  
 Gln Thr Ala Val Arg Ala Gly Thr Val Tyr Val Pro Arg Leu Glu Arg  
 2915 2920 2925  
 40 Ala Ala Asp Arg Thr Asp Gly Pro Leu Thr Pro Pro Asp Asp Gly Ala  
 2930 2935 2940  
 Trp Arg Leu Gly Arg Gly Thr Asp Leu Thr Leu Asp Gly Leu Ala Leu  
 2945 2950 2955 2960  
 45 Val Pro Ala Pro Asp Ala Glu Ala Pro Leu Glu Pro Gly Gln Val Arg  
 2965 2970 2975  
 Val Ala Val Arg Ala Ala Gly Val Asn Phe Arg Asp Ala Leu Ile Ala  
 2980 2985 2990  
 50 Leu Gly Met Tyr Pro Gly Glu Ala Glu Met Gly Thr Glu Gly Ala Gly  
 2995 3000 3005  
 55 Thr Val Val Glu Val Gly Pro Gly Val Thr Gly Val Ala Val Gly Asp  
 3010 3015 3020

Arg Val Leu Gly Leu Trp Asp Gly Gly Leu Gly Pro Leu Cys Val Ala  
 3025 3030 3035 3040  
 5 Asp His Arg Leu Leu Ala Pro Val Pro Asp Gly Trp Ser Tyr Ala Gln  
 3045 3050 3055  
 Ala Ala Ser Val Pro Ala Val Phe Leu Ser Ala Tyr Tyr Gly Leu Val  
 3060 3065 3070  
 10 Thr Leu Ala Gly Leu Arg Pro Gly Glu Arg Val Leu Val His Ala Ala  
 3075 3080 3085  
 Ala Gly Gly Val Gly Met Ala Ala Val Gln Ile Ala Arg His Leu Gly  
 3090 3095 3100  
 15 Ala Glu Val Leu Ala Thr Ala Ser Pro Gly Lys Trp Asp Ala Leu Arg  
 3105 3110 3115 3120  
 Ala Met Gly Ile Thr Asp Asp His Leu Ala Ser Ser Arg Thr Leu Asp  
 3125 3130 3135  
 20 Phe Ala Thr Ala Phe Thr Gly Ala Asp Gly Thr Ser Arg Ala Asp Val  
 3140 3145 3150  
 Val Leu Asn Ser Leu Thr Lys Glu Phe Val Asp Ala Ser Leu Gly Leu  
 3155 3160 3165  
 Leu Arg Pro Gly Gly Arg Phe Leu Glu Leu Gly Lys Thr Asp Val Arg  
 3170 3175 3180  
 30 Asp Pro Glu Arg Ile Ala Ala Glu His Pro Gly Val Arg Tyr Arg Ala  
 3185 3190 3195 3200  
 Phe Asp Leu Asn Glu Ala Gly Pro Asp Ala Leu Gly Arg Leu Leu Arg  
 3205 3210 3215  
 35 Glu Leu Met Asp Leu Phe Ala Ala Gly Val Leu His Pro Leu Pro Val  
 3220 3225 3230  
 Val Thr His Asp Val Arg Arg Ala Ala Asp Ala Leu Arg Thr Ile Ser  
 3235 3240 3245  
 40 Gln Ala Arg His Thr Gly Lys Leu Val Leu Thr Met Pro Pro Ala Trp  
 3250 3255 3260  
 His Pro Tyr Gly Thr Val Leu Val Thr Gly Gly Thr Gly Ala Leu Gly  
 3265 3270 3275 3280  
 45 Ser Arg Ile Ala Arg His Leu Ala Ser Arg His Gly Val Arg Arg Leu  
 3285 3290 3295  
 Leu Ile Ala Ala Arg Arg Gly Pro Asp Gly Glu Gly Ala Ala Glu Leu  
 3300 3305 3310  
 50 Val Ala Asp Leu Ala Ala Leu Gly Ala Ser Ala Thr Val Val Ala Cys  
 3315 3320 3325  
 55 Asp Val Ser Asp Ala Asp Ala Val Arg Gly Leu Leu Ala Gly Ile Pro  
 3330 3335 3340



Ala Asp His Pro Leu Thr Ala Val Val His Ser Thr Gly Val Leu Asp  
 3345 3350 3355 3360  
 5 Asp Gly Val Leu Pro Gly Leu Thr Pro Glu Arg Met Arg Arg Val Leu  
 3365 3370 3375  
 Arg Pro Lys Val Glu Ala Ala Val His Leu Asp Glu Leu Thr Arg Asp  
 3380 3385 3390  
 10 Leu Asp Leu Ser Ala Phe Val Leu Phe Ser Ser Ser Ala Gly Leu Leu  
 3395 3400 3405  
 Gly Ser Pro Ala Gln Gly Asn Tyr Ala Ala Ala Asn Ala Thr Leu Asp  
 3410 3415 3420  
 15 Ala Leu Ala Ala Arg Arg Arg Ser Leu Gly Leu Pro Ser Val Ser Leu  
 3425 3430 3435 3440  
 Ala Trp Gly Leu Trp Ser Asp Thr Ser Arg Met Ala His Ala Leu Asp  
 3445 3450 3455  
 20 Gln Glu Ser Leu Gln Arg Arg Phe Ala Arg Ser Gly Phe Pro Pro Leu  
 3460 3465 3470  
 Ser Ala Thr Leu Gly Ala Ala Leu Phe Asp Ala Ala Leu Arg Val Asp  
 3475 3480 3485  
 Glu Ala Val Gln Val Pro Met Arg Phe Asp Pro Ala Ala Leu Arg Ala  
 3490 3495 3500  
 30 Thr Gly Ser Val Pro Ala Leu Leu Ser Asp Leu Val Gly Ser Ala Pro  
 3505 3510 3515 3520  
 Ala Thr Gly Ser Ala Ala Pro Ala Ser Gly Pro Leu Pro Ala Pro Asp  
 3525 3530 3535  
 35 Ala Gly Thr Val Gly Glu Pro Leu Ala Glu Arg Leu Ala Gly Leu Ser  
 3540 3545 3550  
 Ala Glu Glu Arg His Asp Arg Leu Leu Gly Leu Val Gly Glu His Val  
 3555 3560 3565  
 40 Ala Ala Val Leu Gly His Gly Ser Ala Ala Glu Val Arg Pro Asp Arg  
 3570 3575 3580  
 Pro Phe Arg Glu Val Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg  
 3585 3590 3595 3600  
 Asn Arg Met Ala Ala Val Thr Gly Val Arg Leu Pro Ala Thr Leu Val  
 3605 3610 3615  
 50 Phe Asp His Pro Thr Pro Ala Ala Leu Ser Ser His Leu Asp Gly Leu  
 3620 3625 3630  
 Leu Ala Pro Ala Gln Pro Val Thr Thr Thr Pro Leu Leu Ser Glu Leu  
 3635 3640 3645  
 55 Asp Arg Ile Glu Glu Ala Leu Ala Ala Leu Thr Pro Glu His Leu Ala  
 3650 3655 3660

Glu Leu Ala Pro Ala Pro Asp Asp Arg Ala Glu Val Ala Leu Arg Leu  
3665 3670 3675 3680

5 Asp Ala Leu Ala Asp Arg Trp Arg Ala Leu His Asp Gly Ala Pro Gly  
3685 3690 3695

Ala Asp Asp Asp Ile Thr Asp Val Leu Ser Ser Ala Asp Asp Asp Glu  
3700 3705 3710

10 Ile Phe Ala Phe Ile Asp Glu Arg Tyr Gly Thr Ser  
3715 3720

15 (2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1580 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

25 Met Ala Asn Glu Glu Lys Leu Arg Ala Tyr Leu Lys Arg Val Thr Gly  
1 5 10 15

Glu Leu His Arg Ala Thr Glu Gln Leu Arg Ala Leu Asp Arg Arg Ala  
20 25 30

30 His Glu Pro Ile Ala Ile Val Gly Ala Ala Cys Arg Leu Pro Gly Gly  
35 40 45

Val Glu Ser Pro Asp Asp Leu Trp Glu Leu Leu His Ala Gly Ala Asp  
50 55 60

Ala Val Gly Pro Ala Pro Ala Asp Arg Gly Trp Asp Val Glu Gly Arg  
65 70 75 80

40 Tyr Ser Pro Asp Pro Asp Thr Pro Gly Thr Ser Tyr Cys Arg Glu Gly  
85 90 95

Gly Phe Val Gln Gly Ala Asp Arg Phe Asp Pro Ala Leu Phe Gly Ile  
100 105 110

45 Ser Pro Asn Glu Ala Leu Thr Met Asp Pro Gln Gln Arg Leu Leu Leu  
115 120 125

Glu Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Leu Asp Pro Gln Ser  
130 135 140

50 Leu Ala Gly Ser Arg Thr Gly Val Phe Ala Gly Ala Trp Glu Ser Gly  
145 150 155 160

55 Tyr Gln Lys Gly Val Glu Gly Leu Glu Ala Asp Leu Glu Ala Gln Leu  
165 170 175

Leu Ala Gly Ile Val Ser Phe Thr Ala Gly Arg Val Ala Tyr Ala Leu

## EP 0 791 656 A2

	180	185	190
5	Gly Leu Glu Gly Pro Ala Leu Thr Ile Asp Thr Ala Cys Ser Ser Ser 195 200 205		
	Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly Glu Cys 210 215 220		
10	Asp Leu Ala Leu Ala Gly Gly Ala Thr Val Ile Ala Asp Phe Ala Leu 225 230 235 240		
	Phe Thr Gln Phe Ser Arg Gln Arg Gly Leu Ala Pro Asp Gly Arg Cys 245 250 255		
15	Lys Ala Phe Gly Glu Thr Ala Asp Gly Phe Gly Pro Ala Glu Gly Ala 260 265 270		
	Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His 275 280 285		
20	Pro Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala 290 295 300		
	Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg Val Ile 305 310 315 320		
25	Arg Glu Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp Val Asp Ala 325 330 335		
	Val Glu Ala His Gly Thr Gly Thr Pro Leu Gly Asp Pro Ile Glu Ala 340 345 350		
30	Gly Ala Leu Met Ala Thr Tyr Gly His Glu Arg Thr Gly Asp Pro Leu 355 360 365		
	Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr Gln Ala Ala Ala 370 375 380		
35	Gly Val Ala Gly Val Ile Lys Met Val Leu Ala Leu Arg His Gly Glu 385 390 395 400		
	Leu Pro Arg Thr Leu His Ala Ser Thr Ala Ser Ser Arg Ile Glu Trp 405 410 415		
40	Asp Ala Gly Ala Val Glu Leu Leu Asp Glu Ala Arg Pro Trp Pro Arg 420 425 430		
	Arg Ala Glu Gly Pro Arg Arg Ala Gly Ile Ser Ser Phe Gly Ile Ser 435 440 445		
45	Gly Thr Asn Ala His Leu Val Ile Glu Glu Glu Pro Pro Ala Arg Pro 450 455 460		
50	Glu Pro Glu Glu Ala Ala Gln Pro Pro Ala Pro Ala Thr Thr Val Leu 465 470 475 480		
	Pro Leu Ser Ala Ala Gly Ala Arg Ser Leu Arg Glu Gln Ala Arg Arg 485 490 495		
55			

	Leu	Ala	Ala	His	Leu	Ala	Gly	His	Glu	Glu	Ile	Thr	Ala	Ala	Asp	Ala	
				500					505						510		
5	Ala	Arg	Ser	Ala	Ala	Thr	Thr	Arg	Ala	Ala	Leu	Ser	His	Arg	Ala	Ser	
			515					520					525				
	Val	Leu	Ala	Asp	Asp	Arg	Arg	Ala	Leu	Ile	Asp	Arg	Leu	Thr	Ala	Leu	
		530					535					540					
10	Ala	Glu	Asp	Arg	Lys	Asp	Pro	Gly	Val	Thr	Val	Gly	Glu	Ala	Gly	Ser	
	545					550					555					560	
	Gly	Arg	Pro	Pro	Val	Phe	Val	Phe	Pro	Gly	Gln	Gly	Ser	Gln	Trp	Thr	
					565					570					575		
15	Gly	Met	Gly	Ala	Glu	Leu	Leu	Asp	Arg	Ala	Pro	Val	Phe	Arg	Ala	Lys	
				580					585					590			
	Ala	Glu	Glu	Cys	Ala	Arg	Ala	Leu	Ala	Ala	His	Leu	Asp	Trp	Ser	Val	
			595					600					605				
20	Leu	Asp	Val	Leu	Arg	Asp	Ala	Pro	Gly	Ala	Pro	Pro	Ile	Asp	Arg	Ala	
		610					615					620					
	Asp	Val	Val	Gln	Pro	Thr	Leu	Phe	Thr	Met	Met	Val	Ser	Leu	Ala	Ala	
25		625				630					635					640	
	Leu	Trp	Glu	Ser	His	Gly	Val	Arg	Pro	Ala	Ala	Val	Val	Gly	His	Ser	
					645					650					655		
30	Gln	Gly	Glu	Ile	Ala	Ala	Ala	His	Ala	Ala	Gly	Ala	Leu	Ser	Leu	Asp	
				660					665					670			
	Asp	Ala	Ala	Arg	Val	Ile	Ala	Glu	Arg	Ser	Arg	Leu	Trp	Lys	Arg	Leu	
			675				680						685				
35	Ala	Gly	Asn	Gly	Gly	Met	Leu	Ser	Val	Met	Ala	Pro	Ala	Asp	Arg	Val	
		690				695					700						
	Arg	Glu	Leu	Met	Glu	Pro	Trp	Ala	Glu	Arg	Met	Ser	Val	Ala	Ala	Val	
	705				710					715						720	
40	Asn	Gly	Pro	Ala	Ser	Val	Thr	Val	Ala	Gly	Asp	Ala	Arg	Ala	Leu	Glu	
					725					730					735		
	Glu	Phe	Gly	Gly	Arg	Leu	Ser	Ala	Ala	Gly	Val	Leu	Arg	Trp	Pro	Leu	
				740					745					750			
45	Ala	Gly	Val	Asp	Phe	Ala	Gly	His	Ser	Pro	Gln	Val	Glu	Gln	Phe	Arg	
			755				760						765				
	Ala	Glu	Leu	Leu	Asp	Thr	Leu	Gly	Thr	Val	Arg	Pro	Thr	Ala	Ala	Arg	
		770				775					780						
50	Leu	Pro	Phe	Phe	Ser	Thr	Val	Thr	Ala	Ala	Ala	His	Glu	Pro	Glu	Gly	
	785					790					795					800	
55	Leu	Asp	Ala	Ala	Tyr	Trp	Tyr	Arg	Asn	Met	Arg	Glu	Pro	Val	Glu	Phe	
					805					810						815	

	Ala Ser Thr Leu Arg Thr Leu Leu Arg Glu Gly His Arg Thr Phe Val	820	825	830
5	Glu Met Gly Pro His Pro Leu Leu Gly Ala Ala Ile Asp Glu Val Ala	835	840	845
	Glu Ala Glu Gly Val His Ala Thr Ala Leu Ala Thr Leu His Arg Gly	850	855	860
10	Ser Gly Gly Leu Asp Arg Phe Arg Ser Ser Val Gly Ala Ala Phe Ala	865	870	875
	His Gly Val Arg Val Asp Trp Asp Ala Leu Phe Glu Gly Ser Gly Ala	885	890	895
15	Arg Arg Val Pro Leu Pro Thr Tyr Ala Phe Ser Arg Asp Arg Tyr Trp	900	905	910
	Leu Pro Thr Ala Ile Gly Arg Arg Ala Val Glu Ala Ala Pro Val Asp	915	920	925
20	Ala Ser Ala Pro Gly Arg Tyr Arg Val Thr Trp Thr Pro Val Ala Ser	930	935	940
	Asp Asp Ser Gly Arg Pro Ser Gly Arg Trp Leu Leu Val Gln Thr Pro	945	950	955
25	Gly Thr Ala Pro Asp Glu Ala Asp Thr Ala Ala Ser Ala Leu Gly Ala	965	970	975
	Ala Gly Val Val Val Glu Arg Cys Leu Leu Asp Pro Thr Glu Ala Ala	980	985	990
30	Arg Val Thr Leu Thr Glu Arg Leu Ala Glu Leu Asp Ala Gln Pro Glu	995	1000	1005
	Gly Leu Ala Gly Val Leu Val Leu Pro Gly Arg Pro Gln Ser Thr Ala	1010	1015	1020
	Pro Ala Asp Ala Ser Pro Leu Asp Pro Gly Thr Ala Ala Val Leu Leu	1025	1030	1035
40	Val Val Gln Ala Val Pro Asp Ala Ala Pro Lys Ala Arg Ile Trp Val	1045	1050	1055
	Val Thr Arg Gly Ala Val Ala Val Gly Ser Gly Glu Val Pro Cys Ala	1060	1065	1070
45	Val Gly Ala Arg Val Trp Gly Leu Gly Arg Val Ala Ala Leu Glu Val	1075	1080	1085
	Pro Val Gln Trp Gly Gly Leu Val Asp Val Ala Val Gly Ala Gly Val	1090	1095	1100
50	Arg Glu Trp Arg Arg Val Val Gly Val Val Ala Gly Gly Gly Glu Asp	1105	1110	1115
	Gln Val Ala Val Arg Gly Gly Gly Val Phe Gly Arg Arg Leu Val Gly	1125	1130	1135

Val Gly Val Arg Gly Gly Ser Gly Val Trp Arg Ala Arg Gly Cys Val  
 1140 1145 1150  
 5 Val Val Thr Gly Gly Leu Gly Gly Val Gly Gly His Val Ala Arg Trp  
 1155 1160 1165  
 Leu Ala Arg Ser Gly Ala Glu His Val Val Leu Ala Gly Arg Arg Gly  
 1170 1175 1180  
 10 Gly Gly Val Val Gly Ala Val Glu Leu Glu Arg Glu Leu Val Gly Leu  
 1185 1190 1195 1200  
 Gly Ala Lys Val Thr Phe Val Ser Cys Asp Val Gly Asp Arg Ala Ser  
 1205 1210 1215  
 15 Met Val Gly Leu Leu Gly Val Val Glu Gly Leu Gly Val Pro Leu Arg  
 1220 1225 1230  
 Gly Val Phe His Ala Ala Gly Val Ala Gln Val Ser Gly Leu Gly Glu  
 1235 1240 1245  
 20 Val Ser Leu Ala Glu Ala Gly Gly Val Leu Gly Gly Lys Ala Val Gly  
 1250 1255 1260  
 Ala Glu Leu Leu Asp Glu Leu Thr Ala Gly Val Glu Leu Asp Ala Phe  
 1265 1270 1275 1280  
 25 Val Leu Phe Ser Ser Gly Ala Gly Val Trp Gly Ser Gly Gly Gln Ser  
 1285 1290 1295  
 Val Tyr Ala Ala Ala Asn Ala His Leu Asp Ala Leu Ala Glu Arg Arg  
 1300 1305 1310  
 30 Arg Ala Gln Gly Arg Pro Ala Thr Ser Val Ala Trp Gly Leu Trp Gly  
 1315 1320 1325  
 Gly Glu Gly Met Gly Ala Asp Glu Gly Val Thr Glu Phe Tyr Ala Glu  
 1330 1335 1340  
 35 Arg Gly Leu Ala Pro Met Arg Pro Glu Ser Gly Ile Glu Ala Leu His  
 1345 1350 1355 1360  
 40 Thr Ala Leu Asn Glu Gly Asp Thr Cys Val Thr Val Ala Asp Ile Asp  
 1365 1370 1375  
 Trp Glu His Phe Val Thr Gly Phe Thr Ala Tyr Arg Pro Ser Pro Leu  
 1380 1385 1390  
 45 Ile Ser Asp Ile Pro Gln Val Arg Ala Leu Arg Thr Pro Glu Pro Thr  
 1395 1400 1405  
 Val Asp Ala Ser Asp Gly Leu Arg Arg Arg Val Asp Ala Ala Leu Thr  
 1410 1415 1420  
 50 Pro Arg Glu Arg Thr Lys Val Leu Val Asp Leu Val Arg Thr Val Ala  
 1425 1430 1435 1440  
 55 Ala Glu Val Leu Gly His Asp Gly Ile Gly Gly Ile Gly His Asp Val  
 1445 1450 1455

Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val Arg Met Arg  
 1460 1465 1470

5 Gly Arg Leu Ala Glu Ala Thr Gly Leu Val Leu Pro Ala Thr Val Ile  
 1475 1480 1485

Phe Asp His Pro Thr Val Asp Arg Leu Gly Gly Ala Leu Leu Glu Arg  
 1490 1495 1500

10 Leu Ser Ala Asp Glu Pro Ala Pro Gly Gly Ala Pro Glu Pro Ala Gly  
 1505 1510 1515 1520

Gly Arg Pro Ala Thr Pro Pro Pro Ala Pro Glu Pro Ala Val His Asp  
 1525 1530 1535

15 Ala Asp Ile Asp Glu Leu Asp Ala Asp Ala Leu Ile Arg Leu Ala Thr  
 1540 1545 1550

Gly Thr Ala Gly Pro Ala Asp Gly Thr Pro Ala Asp Gly Gly Pro Asp  
 1555 1560 1565

20 Ala Ala Ala Thr Ala Pro Asp Gly Ala Pro Glu Gln  
 1570 1575 1580

25 (2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1891 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: unknown

30 (ii) MOLECULE TYPE: peptide

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Met Ser Pro Ser Met Asp Glu Val Leu Gly Ala Leu Arg Thr Ser Val  
 1 5 10 15

Lys Glu Thr Glu Arg Leu Arg Arg His Asn Arg Glu Leu Leu Ala Gly  
 20 25 30

Ala His Glu Pro Val Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly  
 35 40 45

Gly Val Ser Thr Pro Asp Asp Leu Trp Glu Leu Ala Ala Asp Gly Val  
 50 55 60

Asp Ala Ile Thr Pro Phe Pro Ala Asp Arg Gly Trp Asp Glu Asp Ala  
 65 70 75 80

50 Val Tyr Ser Pro Asp Pro Asp Thr Pro Gly Thr Thr Tyr Cys Arg Glu  
 85 90 95

Gly Gly Phe Leu Thr Gly Ala Gly Asp Phe Asp Ala Ala Phe Phe Gly  
 100 105 110

55 Ile Ser Pro Asn Glu Ala Leu Val Met Asp Pro Gln Gln Arg Leu Leu

	115	120	125
5	Leu Glu Thr Ser Trp Glu Thr 130	Leu Glu Arg Ala Gly 135	Ile Val Pro Ala 140
	Ser Leu Arg Gly Ser Arg Thr Gly Val Phe Val Gly Ala Ala His Thr 145	150	155 160
10	Gly Tyr Val Thr Asp Thr Ala Arg Ala Pro Glu Gly Thr Glu Gly Tyr 165	170	175
	Leu Leu Thr Gly Asn Ala Asp Ala Val Met Ser Gly Arg Ile Ala Tyr 180	185	190
15	Ser Leu Gly Leu Glu Gly Pro Ala Leu Thr Ile Gly Thr Ala Cys Ser 195	200	205
	Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly 210	215	220
20	Glu Cys Asp Leu Ala Leu Ala Gly Gly Val Ala Val Met Pro Asp Pro 225	230	235 240
	Thr Val Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Val Asp Gly 245	250	255
25	Arg Cys Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala Glu 260	265	270
	Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn 275	280	285
30	Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp 290	295	300
	Gly Ala Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg 305	310	315 320
35	Val Ile Arg Glu Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp Val 325	330	335
	Asp Val Val Glu Ala His Gly Thr Gly Thr Ala Leu Gly Asp Pro Ile 340	345	350
40	Glu Ala Gly Ala Leu Leu Ala Thr Tyr Gly Arg Glu Arg Val Gly Asp 355	360	365
	Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala 370	375	380
45	Ala Ala Gly Val Gly Gly Val Ile Lys Val Val Gln Ala Met Arg His 385	390	395 400
	Gly Ser Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ser Lys Val 405	410	415
50	Glu Trp Ala Ser Gly Ala Val Glu Leu Leu Thr Glu Gly Arg Ser Trp 420	425	430
55	Pro Arg Arg Val Glu Arg Val Arg Arg Ala Ala Val Ser Ala Phe Gly		



	435	440	445
5	Val Ser Gly Thr Asn Ala His 450	Val Val Leu Glu Glu Ala Pro Val Glu 455	
	Ala Gly Ser Glu His Gly Asp Gly Pro Gly Pro Asp Arg Pro Asp Ala 465		475 480
10	Val Thr Gly Pro Leu Pro Trp Val Leu Ser Ala Arg Ser Arg Glu Ala 485		490 495
	Leu Arg Gly Gln Ala Gly Arg Leu Ala Ala Leu Ala Arg Gln Gly Arg 500		505 510
15	Thr Glu Gly Thr Gly Gly Gly Ser Gly Leu Val Val Pro Ala Ala Asp 515		520 525
	Ile Gly Tyr Ser Leu Ala Thr Thr Arg Glu Thr Leu Glu His Arg Ala 530		535 540
20	Val Ala Leu Val Gln Glu Asn Arg Thr Ala Gly Glu Asp Leu Ala Ala 545		550 555 560
	Leu Ala Ala Gly Arg Thr Pro Glu Ser Val Val Thr Gly Val Ala Arg 565		570 575
25	Arg Gly Arg Gly Ile Ala Phe Leu Cys Ser Gly Gln Gly Ala Gln Arg 580		585 590
	Leu Gly Ala Gly Arg Glu Leu Arg Gly Arg Phe Pro Val Phe Ala Asp 595		600 605
30	Ala Leu Asp Glu Ile Ala Ala Glu Phe Asp Ala His Leu Glu Arg Pro 610		615 620
	Leu Leu Ser Val Met Phe Ala Glu Pro Ala Thr Pro Asp Ala Ala Leu 625		630 635 640
35	Leu Asp Arg Thr Asp Tyr Thr Gln Pro Ala Leu Phe Ala Val Glu Thr 645		650 655
	Ala Leu Phe Arg Leu Leu Glu Ser Trp Gly Leu Val Pro Asp Val Leu 660		665 670
40	Val Gly His Ser Ile Gly Gly Leu Val Ala Ala His Val Ala Gly Val 675		680 685
	Phe Ser Ala Ala Asp Ala Ala Arg Leu Val Ser Ala Arg Gly Arg Leu 690		695 700
45	Met Arg Ala Leu Pro Glu Gly Gly Ala Met Ala Ala Val Gln Ala Thr 705		710 715 720
	Glu Arg Glu Ala Ala Ala Leu Glu Pro Val Ala Ala Gly Gly Ala Val 725		730 735
50	Val Ala Ala Val Asn Gly Pro Gln Ala Leu Val Leu Ser Gly Asp Glu 740		745 750
55	Ala Ala Val Leu Ala Ala Ala Gly Glu Leu Ala Ala Arg Gly Arg Arg		

## EP 0 791 656 A2

	755	760	765
5	Thr Lys Arg Leu Arg Val 770	Ser His Ala Phe His 775	Ser Pro Arg Met Asp 780
	Ala Met Leu Ala Asp Phe Arg Ala Val Ala Asp Thr Val Asp Tyr His 785	790	795 800
10	Ala Pro Arg Leu Pro Val Val Ser Glu Val Thr Gly Asp Leu Ala Asp 805	810	815
	Ala Ala Gln Leu Thr Asp Pro Gly Tyr Trp Thr Arg Gln Val Arg Gln 820	825	830
15	Pro Val Arg Phe Ala Asp Ala Val Arg Thr Ala Ser Ala Arg Asp Ala 835	840	845
	Ala Thr Phe Ile Glu Leu Gly Pro Asp Ala Val Leu Cys Gly Met Ala 850	855	860
20	Glu Glu Ser Leu Ala Ala Glu Ala Asp Val Val Phe Ala Pro Ala Leu 865	870	875 880
	Arg Arg Gly Arg Pro Glu Gly Asp Thr Val Leu Arg Ala Ala Ala Ser 885	890	895
25	Ala Tyr Val Arg Gly Ala Gly Leu Asp Trp Ala Ala Leu Tyr Gly Gly 900	905	910
	Thr Gly Ala Arg Arg Thr Asp Leu Pro Thr Tyr Ala Phe Gln His Ser 915	920	925
30	Arg Tyr Trp Leu Ala Pro Ala Ser Ala Ala Val Ala Pro Ala Thr Ala 930	935	940
	Ala Pro Ser Val Arg Ser Val Pro Glu Ala Glu Gln Asp Gly Ala Leu 945	950	955 960
35	Trp Ala Ala Val His Ala Gly Asp Val Ala Ser Ala Ala Ala Arg Leu 965	970	975
	Gly Ala Asp Asp Ala Gly Ile Glu His Glu Leu Arg Ala Val Leu Pro 980	985	990
40	His Leu Ala Ala Trp His Asp Arg Asp Arg Ala Thr Ala Arg Thr Ala 995	1000	1005
	Gly Leu His Tyr Arg Val Thr Trp Gln Ala Ile Glu Ala Asp Ala Val 1010	1015	1020
45	Arg Phe Ser Pro Ser Asp Arg Trp Leu Met Val Glu His Gly Gln His 1025	1030	1035 1040
	Thr Glu Cys Ala Asp Ala Ala Glu Arg Ala Leu Arg Ala Ala Gly Ala 1045	1050	1055
50	Glu Val Thr Arg Leu Val Trp Pro Leu Glu Gln His Thr Gly Ser Pro 1060	1065	1070
55	Arg Thr Glu Thr Pro Asp Arg Gly Thr Leu Ala Ala Arg Leu Ala Glu		

EP 0 791 656 A2

	1075	1080	1085
5	Leu Ala Arg Ser Pro Glu Gly 1090	Leu Ala Gly Val 1095	Leu Leu Leu Pro Asp 1100
	Ser Gly Gly Ala Ala Val 1105	Ala Gly His Pro Gly 1110	Leu Asp Gln Gly Thr 1115 1120
10	Ala Ala Val Leu Leu Thr 1125	Ile Gln Ala Leu Thr 1130	Asp Ala Ala Val Arg 1135
	Ala Pro Leu Trp Val Val Thr 1140	Arg Gly Ala Val Ala Val 1145	Gly Ser Gly 1150
15	Glu Val Pro Cys Ala Val 1155	Gly Ala Arg Val Trp 1160	Gly Leu Gly Arg Val 1165
	Ala Ala Leu Glu Val Pro 1170	Val Gln Trp Gly Gly 1175	Leu Val Asp Val Ala 1180
20	Val Gly Ala Gly Val Arg 1185	Glu Trp Arg Arg Val Val 1190 1195	Gly Val Val Ala 1200
	Gly Gly Gly Glu Asp Gln Val 1205	Ala Val Arg Gly Gly Gly 1210	Val Phe Gly 1215
25	Arg Arg Leu Val Gly Val 1220	Gly Val Arg Gly Gly Ser 1225	Gly Val Trp Arg 1230
	Ala Arg Gly Cys Val Val Val 1235	Thr Gly Gly Leu Gly Gly 1240	Val Gly Gly 1245
30	His Val Ala Arg Trp Leu 1250	Ala Arg Ser Gly Ala Glu 1255	His Val Val Leu 1260
	Ala Gly Arg Arg Gly Gly 1265	Gly Val Val Gly Ala Val 1270 1275	Glu Leu Glu Arg 1280
	Glu Leu Val Gly Leu Gly 1285	Ala Lys Val Thr Phe Val 1290	Ser Cys Asp Val 1295
40	Gly Asp Arg Ala Ser Val 1300	Val Gly Leu Leu Gly Val 1305	Val Val Glu Gly Leu 1310
	Gly Val Pro Leu Arg Gly 1315	Val Phe His Ala Ala Gly 1320 1325	Val Ala Gln Val
45	Ser Gly Leu Gly Glu Val 1330	Ser Leu Ala Glu Ala Gly 1335 1340	Gly Gly Val Leu Gly
	Gly Lys Ala Val Gly Ala 1345	Glu Leu Leu Asp Glu Leu 1350 1355	Thr Ala Gly Val 1360
50	Glu Leu Asp Ala Phe Val 1365	Leu Phe Ser Ser Gly 1370	Ala Gly Val Trp Gly 1375
	Ser Gly Gly Gln Ser Val 1380	Tyr Ala Ala Ala Asn 1385	Ala His Leu Asp Ala 1390
55	Leu Ala Glu Arg Arg Arg 1395	Ala Gln Gly Arg Pro 1400	Ala Thr Ser Val Ala

## EP 0 791 656 A2

	1395	1400	1405
5	Trp Gly Pro Trp Asp Gly Asp Gly Met Gly Glu Met Ala Pro Glu Gly 1410 1415 1420		
	Tyr Phe Ala Arg His Gly Val Ala Pro Leu His Pro Glu Thr Ala Leu 1425 1430 1435 1440		
10	Thr Ala Leu His Gln Ala Ile Asp Gly Gly Glu Ala Thr Val Thr Val 1445 1450 1455		
	Ala Asp Ile Asp Trp Glu Arg Phe Ala Pro Gly Phe Thr Ala Phe Arg 1460 1465 1470		
15	Pro Ser Pro Leu Ile Ala Gly Ile Pro Ala Ala Arg Thr Ala Pro Ala 1475 1480 1485		
	Ala Gly Arg Pro Ala Glu Asp Thr Pro Thr Ala Pro Gly Leu Leu Arg 1490 1495 1500		
20	Ala Arg Pro Glu Asp Arg Pro Arg Leu Ala Leu Asp Leu Val Leu Arg 1505 1510 1515 1520		
	His Val Ala Ala Val Leu Gly His Ser Glu Asp Ala Arg Val Asp Ala 1525 1530 1535		
25	Arg Ala Pro Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val Arg 1540 1545 1550		
	Leu Arg Arg Arg Leu Ala Glu Asp Thr Gly Leu Asp Leu Pro Gly Thr 1555 1560 1565		
30	Leu Val Phe Asp His Glu Asp Pro Thr Ala Leu Ala His His Leu Ala 1570 1575 1580		
	Gly Leu Ala Asp Ala Gly Thr Pro Gly Pro Gln Glu Gly Thr Ala Arg 1585 1590 1595 1600		
35	Ala Glu Ser Gly Leu Phe Ala Ser Phe Arg Ala Ala Val Glu Gln Arg 1605 1610 1615		
40	Arg Ser Ser Glu Val Val Glu Leu Met Ala Asp Leu Ala Ala Phe Arg 1620 1625 1630		
	Pro Ala Tyr Ser Arg Gln His Pro Gly Ser Gly Arg Pro Ala Pro Val 1635 1640 1645		
45	Pro Leu Ala Thr Gly Pro Ala Thr Arg Pro Thr Leu Tyr Cys Cys Ala 1650 1655 1660		
	Gly Thr Ala Val Gly Ser Gly Pro Ala Glu Tyr Val Pro Phe Ala Glu 1665 1670 1675 1680		
50	Gly Leu Arg Gly Val Arg Glu Thr Val Ala Leu Pro Leu Ser Gly Phe 1685 1690 1695		
	Gly Asp Pro Ala Glu Pro Met Pro Ala Ser Leu Asp Ala Leu Ile Glu 1700 1705 1710		
55	Val Gln Ala Asp Val Leu Leu Glu His Thr Ala Gly Lys Pro Phe Ala		

	1715	1720	1725
5	Leu Ala Gly His Ser Ala 1730	Gly Ala Asn Ile Ala 1735	His Ala Leu Ala Ala 1740
	Arg Leu Glu Glu Arg 1745	Gly Ser Gly Pro Ala 1750	Ala Val Val Leu Met Asp 1755 1760
10	Val Tyr Arg Pro 1765	Glu Asp Pro Gly Ala Met 1770	Gly Glu Trp Arg Asp Asp 1775
	Leu Leu Ser Trp Ala 1780	Leu Glu Arg Ser Thr Val 1785	Pro Leu Glu Asp His 1790
15	Arg Leu Thr Ala Met 1795	Ala Gly Tyr Gln Arg 1800	Leu Val Leu Gly Thr Arg 1805
	Leu Thr Ala Leu Glu 1810	Ala Pro Val Leu Leu 1815	Ala Arg Ala Ser Glu Pro 1820
20	Leu Cys Ala Trp Pro 1825	Pro Ala Gly Gly Ala 1830	Arg Gly Asp Trp Arg Ser 1835 1840
	Gln Val Pro Phe Ala 1845	Arg Thr Val Ala Asp 1850	Val Pro Gly Asn His Phe 1855
25	Thr Met Leu Thr Glu 1860	His Ala Arg His Thr 1865	Ala Ser Leu Val His Glu 1870
	Trp Leu Asp Ser Leu 1875	Pro His Gln Pro Gly 1880	Pro Ala Pro Leu Thr Gly 1885
30	Gly Lys His 1890		

#### Claims

1. An isolated DNA molecule consisting of a nucleotide sequence that encodes a polypeptide wherein said polypeptide consists of a platenolide synthase domain.
2. The isolated DNA molecule of claim 1 wherein the nucleotide sequence is selected from the group consisting of: nucleotides 392 to 1603, 1922 to 2995, 3173 to 3424, 3527 to 4798, 5135 to 6208, 7043 to 7597, 7946 to 8197, 8270 to 9541, 9899 to 10909, 10985 to 11530, 12596 to 13153, 13469 to 13720, 14148 to 15422, 15789 to 16844, 16914 to 17510, 18612 to 19166, 19479 to 19730, 20215 to 21486, 21889 to 22872, 23638 to 24159, 24484 to 24678, 24742 to 26016, 26371 to 27381, 27442 to 27966, 28843 to 29892, 29905 to 30462, 30760 to 31002, 31428 to 32696, 33024 to 34022, 34770 to 35327, 35586 to 35837, 36257 to 37528, 37898 to 38905, 39851 to 40408, 40658 to 40909, and 41297 to 41395 all in SEQ ID NO: 1.
3. A polypeptide consisting of an amino acid sequence wherein said polypeptide consists of a platenolide synthase domain.
4. A polypeptide of claim 3 wherein the amino acid sequence is selected from the group consisting of:
  - (a) amino acids 15 to 418, 525 to 882, 942 to 1025, 1060 to 1483, 1596 to 1953, 2232 to 2416, 2533 to 2616, 2641 to 3064, 3184 to 3520, 3546 to 3727, 4083 to 4268, and 4374 to 4457 all in SEQ ID NO: 2;
  - (b) amino acids 35 to 459, 582 to 933, 957 to 1155, 1523 to 1707, and 1812 to 1895 all in SEQ ID NO: 3;
  - (c) amino acids 36 to 459, 594 to 921, 1177 to 1350, 1459 to 1523, 1545 to 1969, 2088 to 2424, 2445 to 2619, 2912 to 3261, 3266 to 3451, and 3551 to 3631 all in SEQ ID NO: 4;

- (d) amino acids 34 to 456, 566 to 898, 1148 to 1333, and 1420 to 1503 all in SEQ ID NO: 5; and  
(e) amino acids 35 to 458, 582 to 917, 1233 to 1418, 1502 to 1585, 1715 to 1747 all in SEQ ID NO: 6.

5. The isolated DNA molecule of claim 1 wherein the nucleotide sequence is selected from the group consisting of:  
nucleotides 392 to 3424, 3527 to 8197, 8270 to 13720, 14148 to 19730, 20215 to 24678, 24742 to 31002, 31428 to 35837, and 36257 to 41395 all in SEQ ID NO: 1.
6. A polypeptide of claim 3 wherein the amino acid sequence is selected from the group consisting of:  
(a) amino acids 15 to 1025, 1060 to 2616, and 2641 to 4457 all in SEQ ID NO: 2;  
(b) amino acids 35 to 1895 in SEQ ID NO: 3;  
(c) amino acids 36 to 1523, and 1545 to 3631 all in SEQ ID NO: 4;  
(d) amino acids 34 to 1503 in SEQ ID NO: 5; and  
(e) amino acids 35 to 1747 in SEQ ID NO: 6.
7. The isolated DNA molecule of claim 1 wherein the nucleotide sequence is selected from the group consisting of:  
nucleotides 350 to 14002, 14046 to 20036, 20110 to 31284, 31329 to 36071, and 36155 to 41830 all in SEQ ID NO: 1.
8. A homogenous preparation of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, and 6.
9. An isolated DNA molecule consisting of nucleotide sequence of SEQ ID NO: 1
10. A recombinant DNA vector comprising the DNA molecule of claim 1.
11. A recombinant DNA vector comprising the DNA molecule of claim 2.
12. A recombinant DNA vector comprising the DNA molecule of claim 5.
13. A recombinant DNA vector comprising the DNA molecule of claim 7.
14. A recombinant DNA vector comprising the DNA molecule of claim 9.
15. A host cell transformed with a recombinant DNA vector of Claim 10.
16. A host cell transformed with a recombinant DNA vector of Claim 11.
17. A host cell transformed with a recombinant DNA vector of Claim 12.
18. A host cell transformed with a recombinant DNA vector of Claim 13.
19. A host cell transformed with a recombinant DNA vector of Claim 14.
20. The recombinant DNA vector deposited under accession number NRRL B-21500.
21. The recombinant DNA vector deposited under accession number NRRL B-21499.

Fig. 1

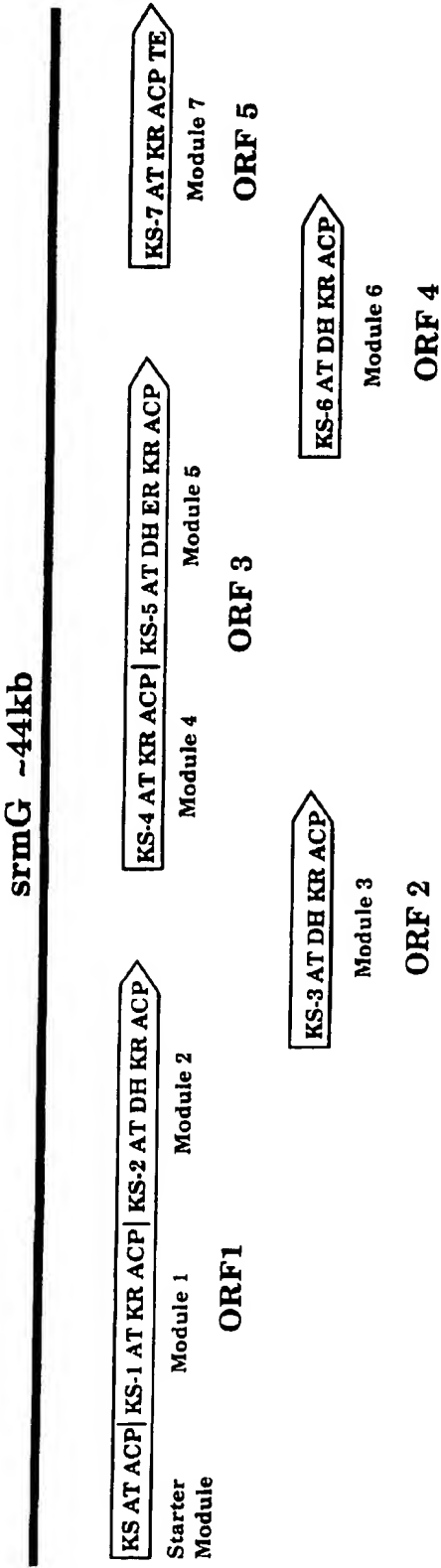


Fig. 2

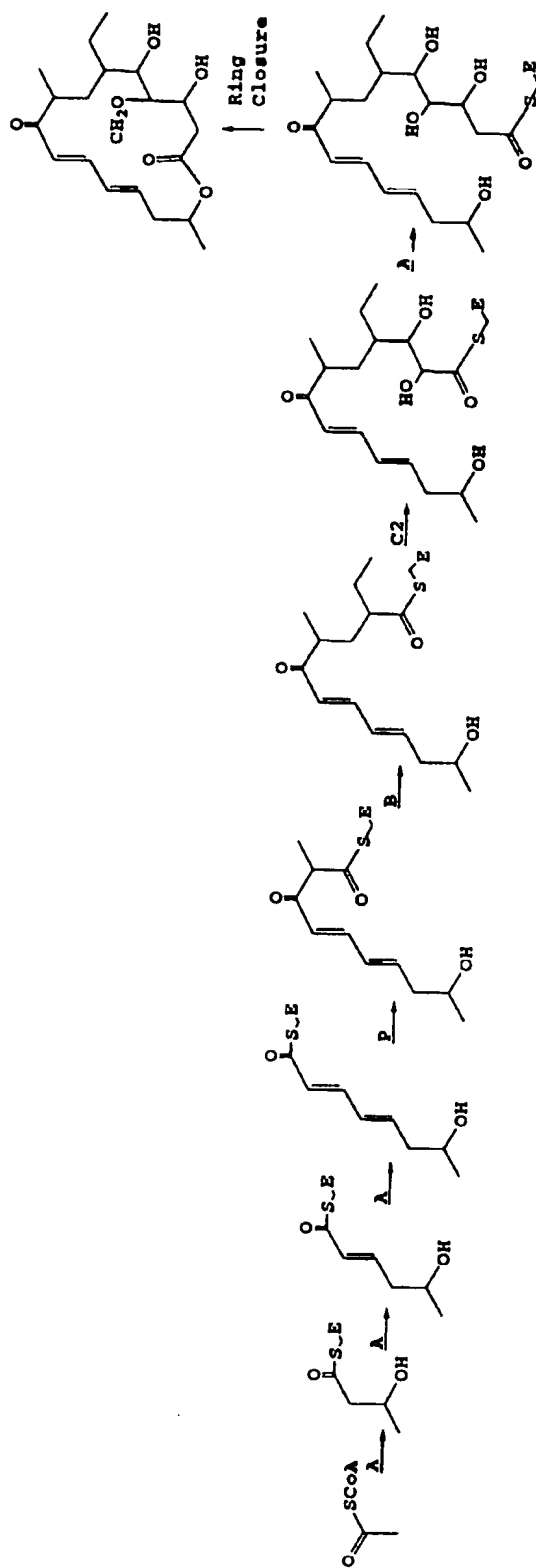
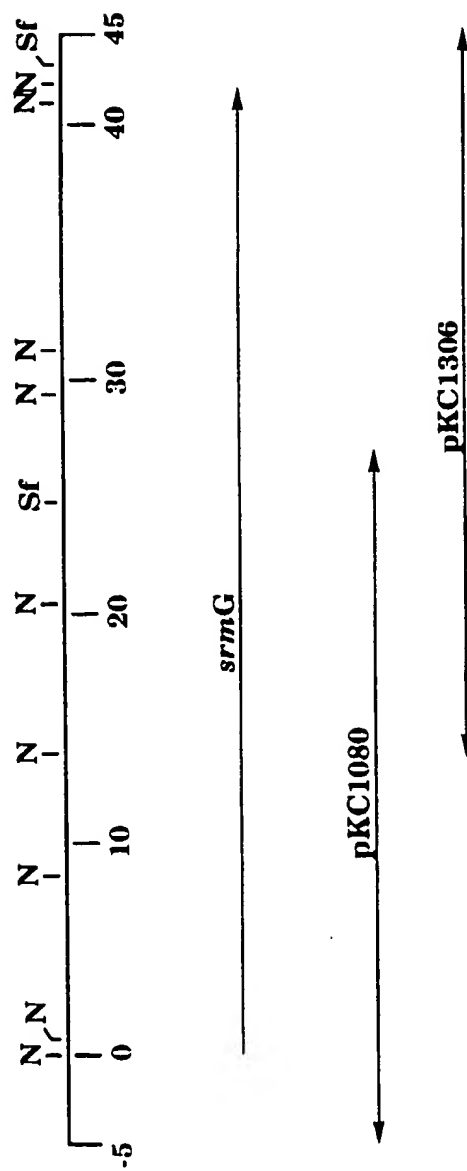




Fig. 3



N = *Nrul*

Sf = *Sful*